Intracranial hypertension after surgical correction for craniosynostosis: a systematic review

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OBJECT The authors' aim was to perform a systematic review on the incidence of intracranial hypertension (IH) after surgery for craniosynostosis.

METHODS A systematic literature review was conducted using PubMed to assess the rate of postoperative IH in studies published between 1985 and 2014. Inclusion criteria were 1) English-language literature; 2) human subjects; 3) pediatric cases; and 4) postoperative IH confirmed with invasive intracranial pressure monitoring.

RESULTS Seven studies met inclusion criteria. IH was reported to be present in 5% of patients postoperatively with sagittal synostosis and 4% of patients with all forms of nonsyndromic craniosynostosis. Inadequate numbers were available to determine the incidence of postoperative IH for syndromic and individual nonsyndromic sutural synostosis based on the inclusion criteria. Surgical groups were subdivided into cranial remodeling procedures without orbital advancement and craniofacial procedures with orbital advancement. IH was reported to be present in 5% of patients with all forms of nonsyndromic sutural stenosis after cranial remodeling procedures and 1% after craniofacial advancement.

CONCLUSIONS Postoperative development of elevated intracranial pressure has been described by multiple institutions, but the variation in how IH is determined and the multiple surgical procedures to correct craniosynostosis has limited the number of studies subject to a meta-analysis. Nonetheless, this entity deserves special attention, and further studies are required to determine the true incidence of postoperative IH, including the role of various surgical procedures on its incidence. The long-term consequences of chronic IH in this group of patients also need to be evaluated.

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KEY WORDS craniosynostosis; intracranial hypertension; cranial vault remodeling; strip craniectomy; intracranial pressure; craniofacial advancement

SINCE Renier et al.²⁷ published their landmark report in 1982, the association between untreated craniosynostosis and elevated intracranial pressure (ICP) has been an extensively debated entity. Renier and colleagues showed that one-third of patients with untreated multisuture synostosis had intracranial hypertension (IH). Other groups have since confirmed these findings of elevated ICP, which differ according to the site of the affected suture—8% in metopic, 13% in sagittal, 16% in unicoronal, and 31% in bicoronal synostosis.^{3,4,20,26}

There is much less consensus regarding the prevalence of IH after surgical remodeling and the consequences of

untreated postsurgical IH. Although isolated reports of elevated ICP following treatment of craniosynostosis exist in the literature, the overall frequency of this entity is underappreciated and underrecognized. Therefore, we completed a systematic review on the incidence of IH following surgical treatment of craniosynostosis.

Methods

Preliminary Search Strategy

The primary objective of the current search strategy was to identify all published studies reporting the inci-

ABBREVIATIONS ICP = intracranial pressure; IH = intracranial hypertension; OCT = optical coherence tomography; RNFL = retinal nerve fiber layer.

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dence of IH after surgical correction for both syndromic and nonsyndromic craniosynostosis. We performed a detailed systematic literature review using the PubMed database. Search results were restricted to studies published between 1985 and 2014. Search criteria were based on key words using the following search terms: “craniosynostosis AND intracranial hypertension” (n = 321) and “craniosynostosis AND intracranial hypertension AND postoperative” (n = 68).

Inclusion and Exclusion Criteria

Inclusion criteria were: 1) English-language literature; 2) human subjects; 3) pediatric cases; and 4) postoperative IH confirmed with invasive ICP monitoring.

Data Collection and Analysis

Primary outcome was the reported incidence of IH after surgical correction for craniosynostosis. Variables included type of craniosynostosis and initial operative procedure.

Results

General Characteristics

Seven studies^{2,7,16–19,30,33} met inclusion criteria for analysis of the primary outcome: incidence of IH after surgery confirmed by invasive ICP monitoring (Table 1). Additional studies that used alternate methods of confirmation of IH were excluded from the analysis but are reviewed in the discussion and included 4 studies using lumbar puncture as confirmation of IH;^{1,6,14,23} 1 study using the presence of papilledema;⁴ and 2 studies used a combination of ICP monitoring, clinical symptoms, and the presence of papilledema^{25,28} (Table 2). One additional study that used invasive ICP monitoring was excluded from analysis because it did not provide adequate information on the total number of monitored patients.⁸ General characteristics of the 7 included studies are reviewed in Table 1. Seven hundred sixty-two patients were reviewed in these studies.

Incidence of Intracranial Hypertension

IH was confirmed with invasive ICP monitoring in all

7 studies (Table 1). In general, the following ICP criteria were used for IH: < 10 mm Hg as normal, 10–15 mm Hg as borderline, and > 15 mm Hg as high, but this was not specified in all studies.

Patients who had undergone surgery for sagittal synostosis had a 5% incidence of postoperative IH based on combined data from 4 studies (Table 3).^{2,7,19,33} The incidence for all nonsyndromic patients was 4% based on 6 studies and included all patients with single or multisutural synostosis.^{2,7,16–19,33} The incidence of IH in syndromic cases was only available in 1 study¹⁸ and was therefore not included in our analysis.

Surgical Intervention

We attempted to further classify incidence of IH by surgical procedure. We were unable to perform an adequate meta-analysis on individual procedures given the extensive variety of surgical interventions that differed by center and type of craniosynostosis (Table 4). As an example, Ceta et al. treated sagittal synostosis with frontal and anterior two-thirds skull reconstruction for the initial 5 years of their study period, after which they switched to a large frontoparietooccipital midline strip craniotomy with extensive bilateral barrel stave osteotomies in the posterior frontal, parietal, temporal, and occipital regions for the remaining cases.⁷ The authors reported an IH rate of 11% for isolated sagittal synostosis but did not distinguish the incidence of IH between the two types of interventions. Marucci et al.¹⁹ and van Veelen et al.³³ used variations of the strip craniectomy for treatment of sagittal synostosis with IH rates of 8% and 9%, respectively. Van Veelen et al.³³ compared 4 versions of the extended craniectomy for sagittal synostosis and found no difference in incidence of elevated ICP between the 4 groups. Arnaud et al.² compared 3 different types of remodeling methods with differing rates of elevated ICP. They noted that the rate of IH was 1% in sagittal synostosis patients treated with the standard “H” craniectomy^{2,11} versus 5% in the non-H craniectomy group. Hudgins et al. reported a 1% incidence of postoperative IH with the “floating” frontoorbital advancement technique for both syndromic and nonsyndromic cases.¹⁹

Given these variations, we performed a subgroup

TABLE 1. Incidence of IH determined by invasive ICP monitoring

Authors & Year	Syndromic/Nonsyndromic	Type	Sample Size	Accrual Time (yrs)	% IH
Cetas et al., 2013	Nonsyndromic	Sagittal	47*	10.5	11%
	Nonsyndromic	Single suture†	81	10.5	6%
Marucci et al., 2008	Nonsyndromic	Sagittal	89	10	8%
Van Veelen et al., 2013	Nonsyndromic	Sagittal	79	7	9%
Arnaud et al., 2009	Nonsyndromic	Sagittal	253	22	1.5%
Hudgins et al., 1998	Nonsyndromic	Single suture†	210	8	1%
Marchac et al., 1988	Syndromic		21	7	38%
	Nonsyndromic‡		14	7	7%
Thompson et al., 1995	Combined syndromic/nonsyndromic		15	15	40%

* These patients are also included in the number of patients with single-suture synostosis.

† All types of single-suture synostosis cases.

‡ Includes both single- and multisuture synostosis.

TABLE 2. Additional studies that address postoperative IH with alternate methods of confirmation

Authors & Year	Syndromic/ Nonsyndromic	Type	Method of IH Confirmation	Sample Size	Accrual Time (yrs)	% IH
Adamo et al., 2010	Nonsyndromic	Sagittal	Lumbar puncture	143	16	1.5%
Cohen et al., 1993	Nonsyndromic	Single suture*	Invasive ICP monitoring	NA	1	NA
Reddy et al., 1990	Nonsyndromic	Single suture*	Combination of ICP monitoring, presence of papilledema, other clinical findings	665†	58	NA
Pollack et al., 1996	Syndromic		Lumbar puncture	22	4	36%
Siddiqi et al., 1995	Syndromic		Combination of ICP monitoring, presence of papilledema, other clinical findings	107	6	6%
Bannink et al., 2008	Syndromic		Presence of papilledema	70	23	43%
Campbell et al., 1995	Syndromic		Lumbar puncture	1‡	NA	NA
Wall et al., 1994	Syndromic		ND	122	14	8%
	Nonsyndromic§		ND	97	14	5%
Foster et al., 2008	Syndromic		Lumbar puncture	13	12.5	15%
	Nonsyndromic§		Lumbar puncture	106	12.5	6%

ND = not documented; NA = not available.

* All types of single-suture synostosis.

† Includes both pre- and postoperative cases.

‡ Single case report.

§ Includes both single- and multisuture synostosis.

analysis on cranial remodeling procedures without orbital involvement (including strip craniectomies) versus craniofacial procedures that included advancement of the orbital rim (Table 5). We combined data from 4 studies^{2,7,19,33} on nonsyndromic patients who had cranial remodeling procedures: 23 of 471 patients (5%) had evidence of IH postoperatively. Combined data from 3 studies^{7,16,18} showed that 3 of 255 nonsyndromic patients (1%) had elevated ICP after craniofacial advancement surgery.

Discussion

Elevated ICP in children does not always present with the classic clinical symptoms of headache, altered consciousness, nausea, and vomiting and therefore often goes undetected with long-term sequelae such as cognitive deterioration and visual loss.^{13,23} Renier et al.²⁷ demonstrated an inverse relationship between ICP and cognitive status in unilateral coronal synostosis, and Arnaud et al.² demonstrated an improvement in behavior and school performance after calvarial remodeling. The progression and

effects of mildly elevated ICP (i.e., with single-suture synostosis) on neonatal cognition and development have yet to be clearly established.⁹ In addition, literature on the long-term neuropsychological consequences of elevated ICP has been indeterminate, with some studies demonstrating evidence that long-term elevated ICP leads to diminished cognition and others showing no effect.²⁹ As a result, there is much debate with proponents of a minimalist approach suggesting that surgical repair of craniosynostosis is mostly for cosmetic purposes and of little functional consequence.

In 2014, Patel et al.²² demonstrated that long-term outcomes in neuropsychological testing were improved when sagittal synostosis was addressed early (prior to 6 months of age); this group also showed that an early complete expansion of the intracranial space with calvarial vault remodeling led to a significant improvement in long-term cognition when compared with a limited correction with a sagittal strip craniectomy.¹⁵ IH may play a role in long-term cognition given that a more extensive calvarial vault remodeling had improved long-term outcomes, but there is a paucity of uniform data in the literature.

The gold standard in the diagnosis of IH is invasive ICP measurement, which can be problematic for 2 reasons: 1) given its invasive nature, it cannot be used as a screening tool, and 2) the lack of a definition of normal ICP in children. For many years, a mean ICP less than 10 mm Hg was considered normal, a mean between 10 and 15 mm Hg borderline, and a mean ICP over 15 mm Hg elevated. However, some experts disagreed with these guidelines and proposed an age-specific system with values of 2 mm Hg in the newborn, 5 mm Hg during infancy, and between 6 and 13 mm Hg for children between 3 and 7 years of age.²¹ Furthermore, ICP can fluctuate over time,

TABLE 3. Literature review: incidence of IH after cranial remodeling

Type of Craniosynostosis	% IH	No. of Studies
Nonsyndromic (26/726 patients)*	4%	6
Sagittal (23/468 patients)	5%	4
Additional sutures	Not enough information for analysis	
Syndromic	Not enough information for analysis	1

* Includes both single- and multisuture synostosis.

TABLE 4. Surgical intervention

Authors & Year	Surgical Approach
Cetas et al., 2013	Sagittal: Frontal/anterior two-thirds skull reconstruction (2000–2004) Frontoparietooccipital midline strip craniectomy w/ 1-cm shortening & barrel stave osteotomies (2005–2010)
Marucci et al., 2008	Sagittal: Modified strip craniectomy
Van Veelen et al., 2013	Sagittal: Extended strip craniectomy (4 different approaches)
Arnaud et al., 2009	Sagittal: Standard H craniectomy Modified H craniectomy w/ removal of coronal suture Non-H craniectomy w/ removal of coronal suture
Hudgins et al., 1998	Single suture: “Floating” frontoorbital advancement
Marchac et al., 1988	Syndromic/nonsyndromic: “Floating” frontoorbital advancement
Thompson et al., 1995	Multiple approaches

and many children with craniosynostosis present with borderline mean ICP (10–15 mm Hg measured during sleep), and therefore patterns in waveforms were also analyzed. In 1960, Lundberg described (in adult patients) Type A plateau waves (increases in ICP > 50 mm Hg lasting several minutes) that are considered abnormal, and Lundberg Type B waves (increases up to 50 mm Hg lasting several minutes) whose clinical significance is still unclear.^{12,13,17} In addition to these inconsistencies in the definition of IH, measurements of ICP have varied between studies. We found only 8 studies that used invasive ICP monitors; additional studies used lumbar punctures or a combination of clinical findings (bulging fontanel/papilledema) and invasive ICP monitoring.

The first major study that measured ICP in patients with untreated craniosynostosis was published in 1982 by Renier et al.²⁷ ICP was monitored in 75 children via an epidural sensor. Twenty-three of 75 patients had obviously increased ICP (> 15 mm Hg), 30 of 75 patients had normal ICP (< 10 mm Hg), and 22 of 75 patients had borderline mean ICP (10–15 mm Hg). The 23 patients with increased ICP had postoperative recordings that showed a decrease of 3 mm Hg (measured in the immediate postoperative period) and 6 mm Hg (measured 6 months after surgery).

Since then, there have been multiple studies looking at the incidence of preoperative intracranial hypertension in patients with craniosynostosis. The reported incidence of elevated ICP in the preoperative period is 8% (metopic craniosynostosis), 13% (sagittal craniosynostosis), 15%

(unicorona craniosynostosis I), 31% (bicoronal craniosynostosis), 47% (multisutural craniosynostosis), 45% (Apert syndrome), and 63% (Crouzon syndrome).⁴

The importance of postoperative surveillance for IH screening has also resurfaced in recent years. Children with syndromic craniosynostoses are generally monitored closely given their comorbidities, and therefore most initial reports of postoperative IH were on these patients. Pollack et al.²³ reported that 36% of their syndromic patients presented with increased ICP (confirmed with lumbar puncture) requiring further surgical treatment, of whom 62% were asymptomatic. Siddiqi et al.²⁸ reported a 6% incidence (confirmed with a combination of ICP monitoring and clinical findings such as papilledema and bulging fontanel) in their syndromic postoperative patients, but their patients were screened only when symptomatic with headaches or irritability, or when they had bulging fontanels on examination. Nonsyndromic cases also require screening for elevated ICP: our meta-analysis showed a 5% incidence of IH in nonsyndromic patients undergoing a cranial remodeling procedure and a 1% incidence in nonsyndromic patients undergoing a more extensive craniofacial procedure. Cetas et al.,⁷ in their recent study, showed a 6% rate of postoperative intracranial hypertension in patients with single-suture synostosis. Their recommendation is that routine funduscopic examination be done annually until patients are 6 years of age.

Nonetheless, the lack of papilledema does not guarantee normal ICP. Tuite et al.³¹ reported on the sensitivity and specificity of papilledema to predict elevated ICP in the pediatric craniosynostosis population: in patients younger than 1 year, papilledema was 25% sensitive and 100% specific for IH. As patients aged, the sensitivity increased (100% in patients older than 8 years) and specificity decreased (88% in patients older than 8 years). Given these findings, a normal funduscopic examination does not equate with normal ICP, especially in patients younger than 8 years. We therefore reviewed additional predictors

TABLE 5. Literature review: incidence of IH with cranial remodeling procedures versus craniofacial advancement procedures

Surgical Approach	% IH	No. of Studies
Cranial remodeling (nonsyndromic) (23/471)	5%	4
Craniofacial procedure (nonsyndromic) (3/255)	1%	3

and potential red flags for IH in the patients postoperatively. Additional indicators of elevated ICP in our review included decreasing head circumference percentiles, bulging fontanel/craniotomy defects, headaches/irritability, and developmental delay.

A common radiological finding often noted in the literature is the copper beaten skull (gyral impressions on the inner table of the skull) seen on both radiographs and CT scans. Tuite et al.,³² in a series of 123 patients with craniosynostosis, noted that presence or absence of the beaten copper skull did not correlate with ICP, and therefore this finding would be an unreliable screening tool.

A potential area of further study is perfusion imaging via either MR or CT imaging. David et al.¹⁰ used SPECT scans to demonstrate perfusion deficits underlying synostotic sutures. These deficits resolved after calvarial remodeling. In a more recent study, 99mTc-ethylcysteinate dimer SPECT imaging was completed both pre- and postoperatively in 85 patients: the mean mental performance quotient (MPQ) scores increased significantly in patients with resolved perfusion defects postoperatively.⁵ There are no published studies utilizing MR and CT perfusion scans to evaluate deficits as a potential predictor for elevated ICP. An additional newly introduced noninvasive test is optical coherence tomography (OCT), which is a noninvasive diagnostic technique for cross-sectional analysis of the optic disc and the retinal nerve fiber layer (RNFL). Patients with papilledema have increased RNFL thickness when compared with patients without papilledema: if these findings are further corroborated, OCT could potentially be used to quantitatively assess early stages of papilledema prior to changes on funduscopic examination.²⁴

We acknowledge that our review is limited given the paucity of studies using invasive ICP monitoring and the variability of both the types of craniosynostosis and surgical approaches. Additionally, the majority of the included studies did not provide information about preoperative and perioperative ICP. We also acknowledge that screening for IH is difficult in this patient population given the low sensitivity of funduscopic examination and imaging in our patient age group. Therefore, our findings likely underestimate the true incidence of IH in craniosynostosis patients after surgical remodeling.

Conclusions

We reviewed 7 studies that documented postoperative IH in a pediatric craniosynostosis population that included more than 700 cases. Reports of elevated ICP after surgical intervention have been increasing over time and appear to be due to improved and additional screening techniques, such as routine annual funduscopic examination and neuroimaging. However, the incidence is still likely underreported due to the low sensitivity of current methods. A reliable noninvasive method is needed to measure ICP to identify pediatric patients with IH following surgical correction of craniosynostosis. A potential noninvasive study is MR/CT perfusion scanning or OCT, which may be able to detect subtle defects prior to the development of observable papilledema. Multicenter studies are needed to accumulate enough data to examine the spectrum of

nonsyndromic and syndromic craniosynostosis and the various surgical procedures to establish the incidence of postoperative IH. Long-term detailed neuropsychological and vision testing is needed to determine the effect of postoperative IH in this patient population.

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