Journal of Cranio-Maxillo-Facial Surgery 45 (2017) 1842–1845

Contents lists available at ScienceDirect

Journal of Cranio-Maxillo-Facial Surgery

journal homepage: www.jcmfs.com

Growth curves for intracranial volume in normal Asian children fortify management of craniosynostosis☆

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ARTICLE INFO

Article history:
Paper received 3 March 2017
Accepted 24 August 2017
Available online 21 September 2017

Keywords:
Intracranial volume
Growth curve
Normal Asian children
Craniosynostosis

ABSTRACT

Background: Although the charting of normal intracranial volume (ICV) is fundamental for managing craniosynostosis, Asian norms in this regard are unknown. The purpose of this study was to establish a growth curve for ICVs in a large series of normal Asian children, providing reference values to guide corrective surgery.
Methods: A total of 124 normal children (male, 63; female, 61) and 41 children diagnosed with craniosynostoses were analyzed. Patients aged 0–8 years presenting to the emergency room and subjected to computed tomography (CT) for head trauma served as the reference cohort. Axial CT head scan data were obtained from radiographic archives at Jichi Medical University. Imaging was done on a Siemens CT scanner (5-mm slice thickness), using a DICOM viewer to measure ICVs.
Results: ICVs were plotted against age, and best-fit logarithmic curves for normal subjects were generated, without and with gender stratification. Male and female growth curves were similar in shape but diverged past the age of 1 year (male > female). ICVs of patients with craniosynostoses were plotted to male and female growth curves by disease subset, revealing the following: sagittal synostosis, near normal (or marginally larger); metopic synostosis, below normal; other non-syndromic synostoses (unilateral, bilateral, and lambdoidal) and Crouzon syndrome, near normal; Apert syndrome, above normal; and Pfeiffer syndrome, variable.
Conclusion: ICVs of early childhood were investigated in Asian subjects, creating growth curves that set criteria for timing, planning and goalsetting in surgical correction of craniosynostosis.

1. Introduction

Craniosynostosis alters the morphology of cranial vault, prevents normal cranial growth, and can elevate intracranial pressure over time. Surgical goals in the event of craniosynostosis are to reduce intracranial pressure and to achieve esthetic cranial contours, but the timing of such surgery is open to debate. Although excess intracranial pressure must be avoided, premature surgical interventions may necessitate secondary revisions. Also, direct attempts to measure intracranial pressure are invasive by design and thus may not be feasible in every case.

Intracranial volume (ICV) is a parameter that can be accurately measured by non-invasive methods, such as computed tomography (CT). ICV correlates with intracranial pressure and may be useful in decisions on appropriate timing of surgery. Few investigators have measured ICV in conjunction with normal growth (Abbott et al., 2000; Kamdar et al., 2009; Sgouros et al., 1999), and none have addressed Asians specifically. Asians are generally less prone to craniosynostosis, compared with Caucasian populations.

The purpose of this study was to establish a standard growth curve for ICV in healthy Asians through large-scale data collection. These growth curves were then extrapolated to Asian patients with craniosynostoses, offering a reference point for needed craniofacial surgery.

☆ Grant: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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http://dx.doi.org/10.1016/j.jcms.2017.08.026
1010-5182/

2. Material and methods

2.1. Patient selection

Children (age range, 0–8 years) presenting at the emergency room of Jichi Medical University Hospital and undergoing CT scans to assess head trauma were eligible for the reference cohort, in the absence of any medical or neurologic disorders. Only those candidates with no significant cranial abnormalities on imaging (124 including 63 males and 61 females) were incorporated in this study. All patients were Japanese and of Asian race. Their ages ranged from 8 days to 8 years.

All patients with craniosynostoses evaluated within the Department of Plastic Surgery at Jichi Medical University from 1996–2010 were analyzed as well (Table 1).

2.2. Data acquisition

Normal cranial imaging data (axial CT views) generated during years 2002–2010 were obtained from the radiographic database at Jichi Medical University Hospital. Studies relied on a Siemens CT scanner (5-mm slice thickness; Siemens AG, Munich, Germany).

2.3. Intracranial volume measurement and data analysis

A DICOM viewer and software (OsiriX; Pixmeo, Bernex, Switzerland) were used to measure ICVs. The intracranial space was defined as the region extending from vertex (cranially) to first axial image of foramen magnum (caudally).

Regions of interest (ROIs) in each slice were determined by manual delineation. Total ICV was calculated by summing cross-sectional areas of intracranial space across all images (maximum slice thickness, 5 mm).

ICVs of 120 normal subjects were plotted against age (in months). The data were further divided by age (Group A: ≤12 months, Group B: 13–24 months, Group C: 25–36 months, and Group D: >36 months). Data in each group were compared by gender, applying unpaired Student's *t*-test. ICVs of patients with craniosynostoses were then plotted to our growth curves by disease subset.

3. Results

Scatter plots of ICV measurements against age (in months) are shown in Fig. 1A, generating a best-fit logarithmic curve: y = 198ln(x)-185.54 (R^2 = 0.76843). Best-fit logarithmic curves are shown by male and female gender in Fig. 1B, becoming y = 180.26ln(x)-128.43 (R^2 = 0.81222) and y = 204.15ln(x) - 171.22 (R^2 = 0.80483), respectively. All values of R^2 were high, so the curves approximated plotted points quite closely. The data show a doubling of ICV from birth to 260 days of age.

Average ICVs by gender in the four age groups of normal subjects were as follows: Group A, 840.8 cc (male) and 774.1 cc (female); Group B, 1137.1 cc (male) and 991.7 cc (female); Group C, 1247.5 cc (male) and 1096.8 cc (female); and Group D, 1356.7 cc (male) and 1225.6 cc (female) (Fig. 1C). Gender differences in the B, C, and D age groups were statistically significant (B: p = 0.00050, C: p = 0.00045, and D: p = 0.00028).

ICVs in patients with sagittal synostoses were nearly the same or were marginally above normal (Fig. 2A). In patients with unilateral synostoses, values were near normal (with one exception) (Fig. 2B), and in instances of bilateral or lambdoidal synostosis, values were essentially normal (Fig. 2C and D). ICVs associated with metopic synostoses were below normal (Fig. 2E). In syndromic patients, values were as follows: Crouzon, normal (Fig. 2F); Apert, above normal (Fig. 2G); and Pfeiffer, variable (Fig. 2H).

The Asian ICV growth curve shows the same trend previously documented in other races, although values ran slight higher after the age of 12 months (Fig. 3).

Table 1
Patients with craniosynostosis evaluated in this study.

Craniosynostosis (subsets)	Patient no.		
	Male	Female	Total
Nonsyndromic			
Sagittal	14	4	18
Unicoronal	4	2	6
Bicoronal	2	2	4
Metopic	2	0	2
Lambdoidal	1	0	1
Syndromic			
Crouzon	3	0	3
Apert	1	3	4
Pfeiffer	3	0	3
Total	30	11	41

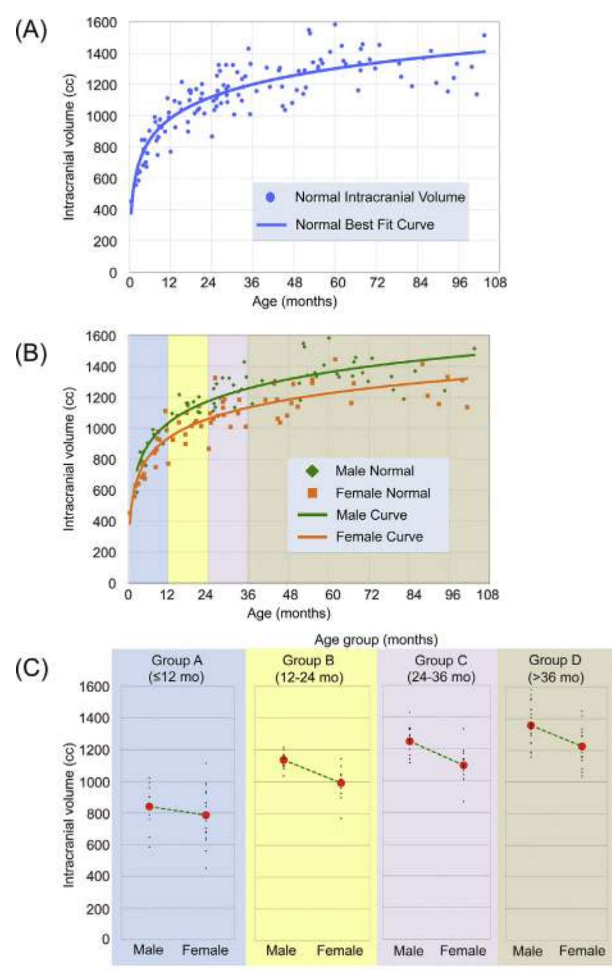

Fig. 1. Intracranial volume of normal Asian children. (A) Scatter plot of normal intracranial volumes by age (in months), with best-fit logarithmic curve of y = 198ln(x)-185.54 (R^2 = 0.76843). **(B)** Scatter plot of normal intracranial volumes by age (in months), with best-fit logarithmic curves of y = 180.26ln(x)-128.43 (R^2 = 0.81222) in male subjects and y = 204.15ln(x)-171.22 (R^2 = 0.80483) in female subjects. **(C)** Data plotted incrementally by age as Group A (≤12 mo, blue), Group B (13–24 mo, yellow), Group C (25–36 mo, purple), and Group D (>36 mo, brown) for gender comparisons (unpaired Student's *t*-test applied).

4. Discussion

Surgical goals in correcting craniosynostosis are of functional and esthetic importance. The functional aspect is to ensure sufficient space for brain growth, avoiding heightened intracranial pressure. The esthetic intent is to impart a naturally shaped cranial vault. To this end, establishing a normal ICV growth curve provides a useful reference.

In our comparisons of ICVs in normal male and female subjects, the growth curves were similarly shaped. However, beyond 1 year of age, ICV values diverged significantly by gender (male>female), which was substantiated in ICV growth curves generated by previous reports on other races (Abbott et al., 2000; Sgouros et al., 1999). These results indicated that it is better to use each ICV growth curve by gender in evaluating the need for surgery in infants (>1 year) with craniosynostosis.

Head circumference is easily measured and its data in Japanese children reported previously (Anzo et al., 2002) showed a very similar growth curve to the ICV growth curve of this study. Head circumference may serve equally in monitoring growth, although correlation between head circumference and ICV in skull deformities remains unknown.

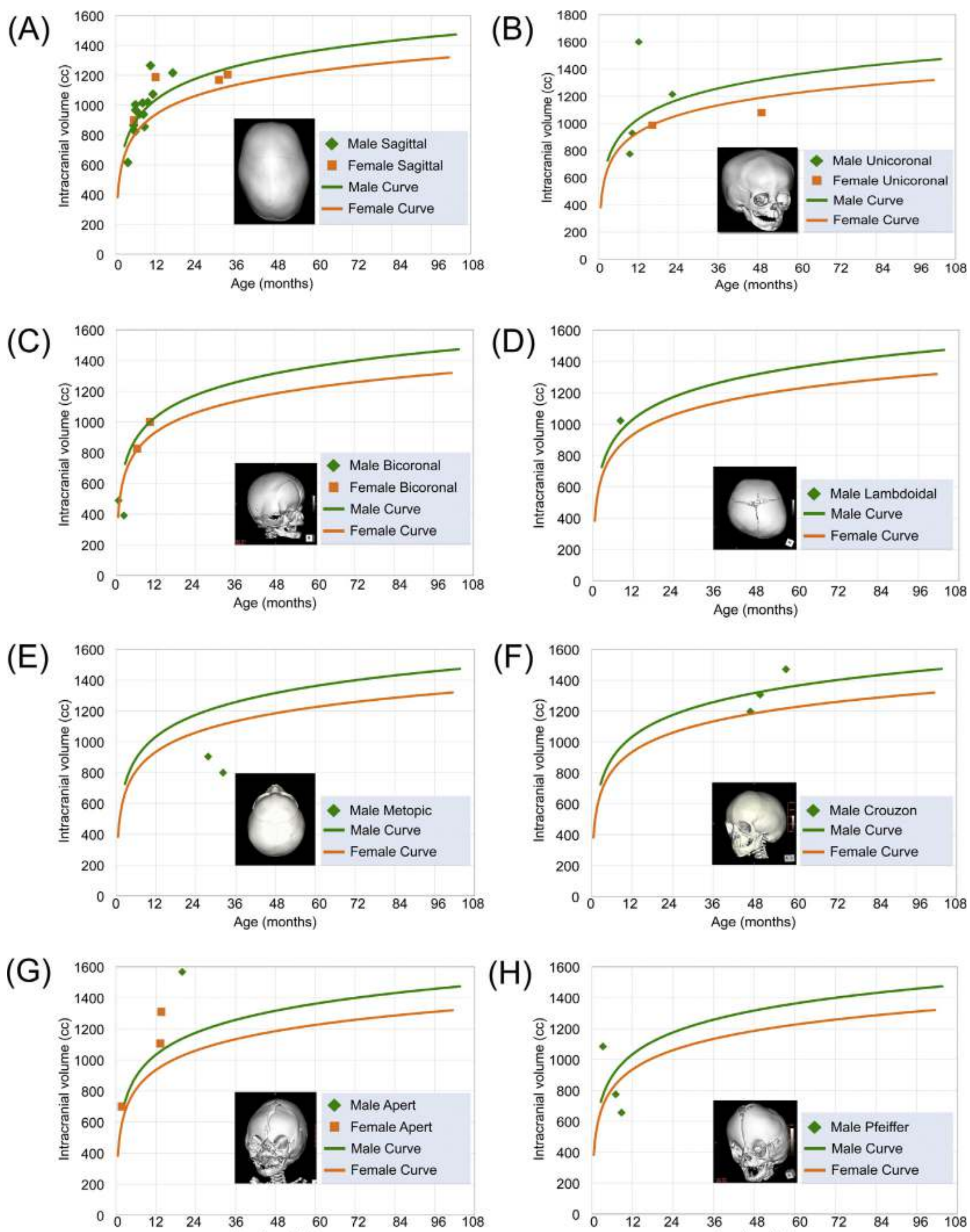

Fig. 2. Intracranial volumes of Asian patients with craniosynostoses plotted to normal male/female growth curves by disease subsets: **(A)** sagittal, **(B)** unicoronal, **(C)** bicoronal, **(D)** lambdoidal, and **(E)** metopic synostoses; and **(F)** Crouzon, **(G)** Apert, and **(H)** Pfeiffer syndromes. A 3D-CT image of a typical case is also shown in the graphs.

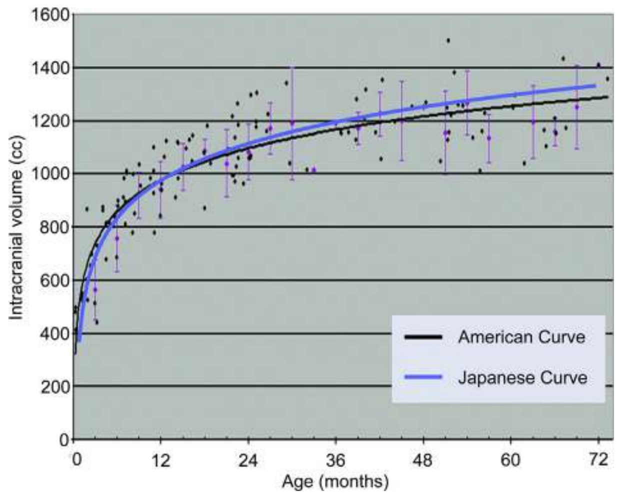

Fig. 3. Best-fit logarithmic approximation of intracranial volumes in normal Asian children relative to American norms. The ICV curve of Japanese children is shown as a blue line which plotted data, and the ICV curve of American children in black, cited and revised from Ref. #1 by Kamdar et al.

Because ICV is rather easily ascertained from CT images, its utility in gauging the timing and goals of surgery seem obvious. However, there is also a question of radiation exposure. For this reason, it may be worth searching for alternative techniques, such as 3D photogrammetry or magnetic resonance imaging (MRI), by which to obtain this vital measurement.

The ICV growth curve created here for Asian children parallels curves previously reported for other races (Abbott et al., 2000; Kamdar et al., 2009; Sgouros et al., 1999), while trending slightly higher in values (Fig. 3). The shapes are consistent, even if overall brain volume in Asians was reported to differ slightly with respect to White and Black races (Rushton and Ankney, 1996). Patients that Kamdar et al. and Sgouros et al. have analyzed were racially mixed (Kamdar et al., 2009; Sgouros et al., 1999), so the slight deviation mentioned above is not untoward. Nevertheless, it underscores that when evaluating craniosynostoses in Asian patients, it is best to use the Asian ICV growth curve.

Our data showed that ICV values in instances of sagittal, lambdoidal, and unicoronal synostoses were nearly the same or were a bit larger than those of the normal population. These results are aligned with prior reports, asserting that ICVs are not below normal in patients with sagittal or unicoronal synostoses (Anderson et al., 2007; Netherway et al., 2005). Hence, corrective surgery in such patients is primarily aimed at cosmesis, improving symmetry and natural shaping of cranial vaults.

In terms of cranial growth, the appropriate timing of surgery is still debatable. There are two opinions on this matter: early (in first few months of life) or late (towards end of first year). It seems likely that if ICVs are normal (as in patients with sagittal, unicoronal, or lambdoidal synostoses), early intervention is not required. On the other hand, some investigators have shown that intracranial pressure is independent of cranial volume. Arnaud et al. have cited a 13.4% incidence of elevated intracranial pressure by 1 year of age in patients with sagittal synostoses (Arnaud et al., 1995); and according to Wall SA et al., this rate is much higher (44%) (Wall SA et al., 2014). Even if ICV is not problematic, neurologic findings must be periodically monitored.

ICVs in patients with bicoronal synostoses did not differ from established norms, but the small number and limited age of our male patients were insufficient for accurately projecting ICV by logarithmic curve. Regarding Apert syndrome, values were above normal in our patients; and Sgouros recorded higher than normal ICVs in patients with Apert syndrome past the age of 6 months (Sgouros, 2005).

In patients with metopic synostoses, we found that ICVs were below normal. This observation is corroborated by Netherway et al., who reported that the ICVs of males >7 months old with metopic synostoses were significantly below normal (Netherway et al., 2005). Anderson et al. have also confirmed that male patients with metopic synostoses display ICVs below normal (Anderson et al., 2004). In this context, ICV may truly provide a means to guide the timing and strategy of corrective surgery.

Our ICV determinations in instances of Pfeiffer syndrome varied. In two patients with cloverleaf skull and multi-suture synostoses, ICVs were below normal; whereas in another patient with poor brain development due to hydrocephalus, ICV was excessive. Here as well, the ICV growth curve may prove beneficial for surgical goal-setting. Early surgery (in first few months of life) may be indicated if values are clearly below normal. Given the relatively small sampling of patients with deformities analyzed herein, the potential for bias certainly exists.

5. Conclusion

Growth curves generated from ICV determinations in normal Asian children offer a valuable reference for timing, planning and goal-setting of corrective surgery in patients with craniosynostoses. Because the curves diverge by gender, they must be properly applied.

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