What Can a Morphometric Study of Unoperated Children Teach Us About The Natural History of Metopic Synostosis?

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Abstract:

Background: Outcomes of surgical repair of trigonocephaly are well-reported in the literature, however there is a paucity of information on the natural history of unoperated children. We evaluated a group of unoperated children with metopic synostosis to describe the natural change in head shape over time.

Methods: We screened our database for scans of children with unoperated trigonocephaly (2011-2021). Multisutural cases and metopic ridge were excluded. 3D surface scans (3D stereophotogrammetry/CT) were used for morphological analysis. 9 previously published parameters were used: frontal angle (FA_{30}), antero-posterior volume ratio (APVR), antero-posterior area ratio (APAR), antero-posterior width ratio 1 and 2 (APWR1 and APWR2), and 4 antero-posterior diagonal ratios ($rAPDR_{30}$, $lAPDR_{30}$, $rAPDR_{60}$, $lAPDR_{60}$).

Results: 97 scans were identified from a cohort of 316 single metopic patients, in which the male to female ratio was 2.7:1. Age at scan ranged from 9 days to 11 years and was stratified into 4 groups: group 1, <6 months; group 2, 6-12 months; group 3, 1-3 years; group 4, >3 years. Significant improvements were detected in 5 parameters (APVR, APAR, APWR1, rAPDR30, lAPDR30) over time, whereas no significant differences were found in FA30, APWR2, rAPDR60, and lAPDR60 between age groups.

Conclusion: forehead shape (surface area and volume), as well as narrowing and anterolateral contour at the frontal points, differed significantly over time without surgery. However, forehead angulation, narrowing, and anterolateral contour at temporal points did not show significant difference. This knowledge will aid in surgical and parental decision making.

Introduction:

Fusion of the metopic suture normally occurs during the first year of life. It begins at the nasion and proceeds superiorly [1]. Premature (in-utero) fusion (metopic synostosis) results in the development of a typical triangular head shape (trigonocephaly) with a prow-shaped midline "keel", frontotemporal constriction, parieto-occipital widening and hypotelorism [2]. Trigonocephaly has been traditionally treated with a fronto-orbital reconstruction (FOR), for many years a well-established procedure [3] for achieving an improved head shape – both subjectively [4, 5] and objectively [6], despite concerns about a predisposition to late-developing deformities [4, 7.] More recently, endoscopic strip craniectomy with postoperative helmet orthosis therapy (ESCH) has been proposed as an alternative to FOR [8, 9].

The natural history of the unoperated metopic synostosis head shape has received little attention, with studies focussed more on the condition's cognitive and developmental sequelae than the children's appearance [2, 10-13]. In 1981 Dominguez et al [14] described (and illustrated with serial radiographs) dramatic spontaneous improvement in "*hypotelorism, keel-shaped forehead and ovoid orbits with parallel long axes*" in children with metopic synostosis who had not undergone surgery and had been followed up for a mean period of 9 years. They concluded that "*Uncomplicated trigonocephaly appears to be a benign self-correcting deformity of uncertain aetiology that does not require surgery for clinical management.*" The senior authors of the present report have also had experience of subjects whose early photographs showed convincing evidence of trigonocephaly that appeared over several years to have improved spontaneously. The contrary view – that trigonocephaly does not improve with time – has also been advanced [15, 16]. Several studies [5, 17, 18] have reported how in children with metopic synostosis there is, post-FOR, an above-normal acceleration of frontal growth that results in a reduction in the degree of hypotelorism. This has however been attributed to the surgery.

The aim of the present study was to use a previously described morphometric method [19] to analyse 3D CT and stereophotogrammetry-derived (SPG) surface scans of a series of children of different ages born with metopic

synostosis but who had not undergone any form of surgical intervention in order to determine what, if any, changes in head shape might occur spontaneously.

Methods:

Our institution's electronic patient record was searched for patients registered between January 2010 and November 2021 using the terms 'metopic synostosis', 'single suture metopic', 'trigonocephaly.' Excluded were children with other cranial suture synostosis and those with a metopic ridge in the absence of trigonocephaly. Date of birth, gender, management decision (operative or non-operative) and age at scanning were recorded. When a patient's family had opted for surgery and a waiting list entry had been made, that child was classified as operatively managed, regardless of whether surgery had been completed by the time of the study. We included all children with scans, either from 3D CT skin reconstructed images or from 3D stereophotogrammetry scans (3dMDHead system; 3dMD, Atlanta, GA, USA), that were of sufficient quality to undergo the morphometric analyses detailed below. In order to study the "unoperated" scans, we included scans -regardless of severity of the deformity - who were either for conservatively managed patients or were obtained before having any surgical intervention.

3DSPG scans: Scans from the camera station were imported as stereolithography (STL) files into a 3D analysis workstation on which a variety of 3D analysis software was available. The scans were registered and trimmed using a previously published method [19] except that the ears (which lie above the base plane) were removed using Materialise 3-Matic version 15 (Materialise; Leuven, Belgium) to allow a more precise measurement of surface areas and intracranial volumes.

CT scans: After application of the inclusion and exclusion criteria the entire CT studies of the remaining eligible patients were downloaded as anonymized DICOM files. These were then imported into Mimics Medical software (Materialise; Leuven, Belgium) for reconstruction and segmentation into soft tissue 3D images. The

reconstructed images were then exported as STL files for processing using the same method as for the 3DSPG scans.

Morphological analysis: Vector measurements were taken at 12 landmark points resembling a clock face (Figure 1, A). 9 previously described [19] parameters were used for the morphological analysis of the deformity (Figure 1). Ratios were calculated to eliminate the effect of normal physiological growth. A list of parameters used, and their significance are in (Table 1) [19, 20, 21].

Normative values and defining 'improvement.': Control values (obtained from scans of children without craniofacial deformity) were used from a previous study [19] to define 'normal' head shape. Improvement was defined as a result that moved closer to those values.

All measurements in this study were conducted by the first and second authors, identified as AE and LS. AE is a fellow in paediatric neurosurgery, while LS holds expertise as a design engineer. To assess the agreement between their measurements, the Intraclass Correlation Coefficient (ICC) was calculated, resulting in a value of 0.97.

Statistical analysis: For continuous dependent variables, Kruskal Wallis test (non-parametric ANOVA) was used to compare the 4 age groups. Subsequently, in the event of obtaining statistically significant results, post hoc pairwise comparisons were utilized to determine which groups differ from each other group. Pearson Chi-Square was used for nominal variables. The p-value was considered significant if $P < 0.05$. SPSS (v26, IBM, USA) and Excel 365 (Microsoft, USA) were used for the statistical analyses.

Ethical Statement: All scans (CT or 3DSPG) used in the study were acquired as part of routine clinical practice and appropriate informed consent was taken as part of standard follow-up. No patient identifiable data or

features were revealed. As this is a retrospective study not requiring extra scans or data collection or use of patient identifiable data it was registered as a Clinical Audit in our institution with all ethical and scientific approval from the Clinical Governance Committee.

Results:

An initial records search delivered 347 patients of whom 31 were excluded because their final diagnosis included 'Benign metopic ridge.' Of the remaining 316 (231 male; 85 female; ratio 2.7:1) 192 (60.8%) had at the time of entry to the study undergone some form of surgical treatment (FOR or ESCH, the latter which has been offered at our institution since 2017 [22]). No significant correlation was found between gender and surgical versus non-surgical management (P = 0.344).

107 of the 316 children were eligible for the study (those who had had either 3D CT or SPG surface scans prior to any surgery) of whom 10 were excluded (regardless of their management method or severity of the deformity) as the scans did not meet quality criteria for analysis. The remaining 97 studies were subjected to the 3D morphological analysis described above (Figure 2). These subjects were then divided into 4 Groups according to their age at scanning (overall range 9 days to 11 years; median 9.6 months): Group 1: < 6 months; Group 2: 6-12 months; Group 3: 1-3 years; and Group 4: > 3 years (range (3.4-11 years; median 5 years). (Table 2)

No significant difference was found in the frontal angle (FA_{30}) between any of the age Groups (a mean of 118.2º for Group 1 and 121.8º for Group 4, for example). APVR (the frontal to parietal volume ratio) was significantly smaller for children in Group 1 (mean = 0.80) compared to those in Group 4 (mean = 0.84; P =0.016). APAR (the frontal to parietal surface area ratio) was also significantly greater in older children – between Group 1 and Group 3: p=0.002; between Group 1 and Group 4: p=0.000; between Group 2 and Group 4 (p=0.024). Ratios of measurements at frontal points ($APWR_1$, $rAPDR_{30,}$ and $lAPDR_{30}$) between Group 1 and Group 4 also

increased significantly (p=0.047, p=0.031, and p=0.031 respectively). Measurements at the temporal points ($APWR_2$, $rAPDR_{60}$, and $lAPDR_{60}$) showed no significant differences between the age groups. Results are summarised in (Table 3).

To determine whether the youngest children (< 1 year) (Groups 1 & 2) formed a homogenous group with regard to the severity of their trigonocephaly, they were divided into those who were later selected for surgery and those who were not. Their frontal angles (taken as an index of severity of their trigonocephaly) were measured and no statistical difference found between the operative and non-operative groups (p = 0.176) (Figure 3). Furthermore, we conducted a detailed examination of the ages at which the oldest children, whose scan ages ranged from 5 to 11 years, initially presented to the craniofacial service. In all patients except one, the ages at initial presentation were younger than the ages at which the scans were conducted.

The mean of the vector measurements of each of the 12 landmarks was calculated for Groups 1 and 4, and the difference between them determined (Figure 4). There was no significant difference overall between the anterior (P.10,11,12,1,2) and posterior landmark measurements (P.4,5,6,7,8) between these two groups. The greatest differences in the frontotemporal region were seen at P.12 (22 mm), followed by frontal points P.1 and P.11 (both 20 mm) and temporal points P.2 and P.10 (15 mm and 14 mm, respectively).

Discussion:

One of the most common questions encountered in the craniofacial clinic from parents of an infant diagnosed with trigonocephaly is ‘what will happen if we do not operate?’ and it is not uncommon for requests to be made to see photographs of unoperated older children. Equally, evaluation of a therapy is only of practical use when set against a condition’s natural history. However, despite this need, there is a lack of published data on the natural history of unoperated trigonocephaly, and the data that is available is contradictory, with some groups reporting improvement [14], some no change [15, 16] and others a mixed outcome [17]. Whilst improvement in hypotelorism has been consistently reported over time [5, 18] it remains unclear whether this is the natural history

of the condition or the result of early remodelling surgery. In this study we shoe, using morphological analysis of 3D surface scans, how the frontal supra-orbital narrowing component of the trigonocephalic deformity of children with unoperated metopic synostosis improves over time. From the children's first to fifth years (Groups 1 and 4) there is a spontaneous widening not only of the frontal regions but a significant increase in the volume and surface areas of the forehead when compared to the posterior cranium. However, this occurs in the absence of any improvement of the frontal angle (FA_{30}) and the more lateral narrowing at the temporal region. The lack of significant difference between Groups 1 and 4 in the anterior (P.10,11,12,1,2) measurements compared to the posterior (P.4,5,6,7,8) indicates how the fronto-temporal regions and the parieto-occipital regions change at same rate over this period, even as changes in their ratios indicated fronto-temporal widening.

In regards to hypotelorism, this study has taken the improvement in the bifrontal width (Figure 1, C) as a proxy for more direct index such as the interorbital width which has been reported by other groups to spontaneously improve [5, 14, 17]. We have interpreted the increase in the ratios of growth recorded between anterior and occipito-parietal regions ($APWR_1$, $rAPDR_{30}$, and $lAPDR_{30}$ and $APWR_2$, $rAPDR_{60}$, and $lAPDR_{60}$) as indicating how, without surgery, children with trigonocephaly can expect over their first five years spontaneous improvement in the hypoteloric aspect of their deformity.

Our results also showed significant change in the volume of the forehead compared to the parieto-occipital region in all age groups. Cronin et al also used 3D CT to evaluate whole head volumes in 72 metopic synostosis patients under the age of 1 year. They found it started significantly lower compared to normal controls but increased to reach normal values by the age of one year – the period of most rapid head growth [23]. The difference in age range at which such spontaneous improvements occur (one year versus some five years) between that study and our series is likely explained by their use of whole head volumes rather than comparing forehead to posterior half of the head (APVR) volumes – which we submit would provide a more realistic assessment of spontaneous change in children with unoperated trigonocephaly.

We identified how the frontal and temporal regions in untreated metopic synostosis grow at different rates with growth at the most anterior point (P.12) showing the greatest difference between Group 1 and Group 4, followed by frontal points (P.1 and P.11) and then temporal points (P.2 and P.10) (Figure 4). These changes occurred without significant opening up of the frontal angle (FA_{30}) – a metric frequently taken as a measure of the severity of trigonocephaly using a variety of imaging techniques [6, 21] – despite such parameters as $APWR_1$, $rAPDR_{30}$, and $lAPDR_{30}$ including measurements taken from the frontal point. This apparent disparity is explained by the apex of the frontal triangle (Figure 1; P12) advancing at a rate dictated by that of frontal bone growth (at Figure 1; P1 & 11), to leave the forehead overall widened but with the same central contour.

It is possible from this study to identify three patterns of trigonocephaly in unoperated children with metopic synostosis: 1) frontotemporal (the most common; where narrowing extends to the temporal landmarks and both $APWR_1$ and $APWR_2<0.90$); 2) bifrontal where narrowing is greater at the frontal landmarks and $APWR_1< 0.90 <APWR_2$); and 3) bitemporal (the least common, where narrowing is greatest at the temporal landmarks and $APWR_2<0.90<APWR_1$) (Figure 5). Such a classification has implications for selecting which children with metopic synostosis are likely in the long-term to benefit most from surgery – and from which procedure. It could, for example, be predicted that as the frontal landmarks show most spontaneous improvement, those children in whom bifrontal narrowing is most evident are more likely to benefit from non-operative management while those in whom the temporal this area is most affected (the bi-temporal or frontotemporal types) are less likely to improve without surgical correction. This observation of different phenotypes (e.g more frontal prominence vs more lateral recession) is often made subjectively by the surgeon in clinic, but further longitudinal studies are required to assess whether or not these patterns predict long-term outcomes for individual patients.

Surgical decisions also need to take into account the possibility that surgery (FOR or ESCH) might itself lead to deformities of their own. It is now well recognised that FOR may predispose to such late-developing deformities as the fronto-temporal indentations that have been attributed in part to deficiency of the upper

elements of temporalis in the affected areas [7, 24] and whose incidence increases with the length of follow-up [4]. Whether ESCH also carries such future risks requires longer-term appearance-focussed studies than presently available but in theory the omission of temporalis muscle dissection could lead to their prevention.

There are limitations to the current study. We have used two-dimensional measurements to describe changes in a 3-dimensional object – the trigonocephalic deformity of unoperated children with metopic synostosis. While many morphometric studies [5, 18] are based on linear width measurements, it is our opinion that as the triangular deformity is most obvious in the axial plane, the degree of frontal indentation is best characterized by ratios of the 30º and 60º vectors (Figure 1) – the lowest ratio being for where the deformity it is most obvious and the surface landmarks retracted medially and posteriorly.

The ideal study to describe change over time in children with untreated metopic synostosis would be longitudinal with the same imaging modality used for the same children and repeated at set intervals. The present study is however based on single time-point data derived from single subject at different ages. It is therefore open to the criticism that morphometric improvements observed in older children represent no more than those subjects were from the outset more mildly affected and were conservatively managed because of this. In brief, their improved indices might reflect no more than persistence of their original – lesser – deformity. However, we did not see a statistical difference in severity in the Group 1 patients between those whose parents opted for surgery and those who chose conservative management, suggesting that this is not the case.

The accelerated growth rate in frontal width we observed during the first three years or so of life mirrors what has been reported in other studies [5, 18] – although attributed by them to the FOR their subjects had previously undergone. The data from our unoperated cases suggests however that such changes are more likely due to the natural history of the condition than any effect of surgery. Finally, the disparity between the improvements we have recorded in some parameters (frontal width, for example) while another (the frontal angle) remains the same suggests that what occurs during childhood is a spontaneous process of "correction" of the trigonocephalic deformity proceeding unevenly rather than persistence of the original shape.

Conclusion:

This is the first study to use data from 3D surface scans to quantify morphological differences in unoperated metopic synostosis children among different age groups. Overall forehead shape as represented by its frontal width, its volume and its surface area differed significantly in unoperated children over the age range covered by this study – the first to fifth years. The frontal angle and temporal narrowing however did not show significant difference. Whether this particularly unsightly aspect of the trigonocephalic deformity can also improve spontaneously requires follow-up studies to at least the age of ten years.

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Figure Legend:

Figure 1: **A**: Bird's-eye view shows the origin point (P.0) and radial vector indicators intersecting the head contour at 12 o'clock–like arranged landmarks. **B**: Frontal Angle (FA_{30}) between the most anterior point of the forehead (P.12), P.1 and P.11. **C**: anteroposterior width ratio1 ($APWR_1$) (dashed/solid). **D**: anteroposterior width ratio2 ($APWR_2$) (dashed/solid) **E**: Right 30º diagonal ratio ($rAPDR_{30}$) (dashed/solid). **F**: Left 30º diagonal ratio ($lAPDR_{30}$) (dashed/solid). **G**: Right 60º diagonal ratio ($rAPDR_{60}$) (dashed/solid). **H**: Left 60º diagonal ratio ($rAPDR_{60}$) (dashed/solid).

Figure 2: A flowchart illustrating the procedural sequence for the selection of 3D scans that have undergone morphological analysis.

Figure 3: Box and Whisker chart of the non-improving parameters: A: FA_{30} (A), $APWR_2$, $rAPDR_{60}$, $lAPDR_{60}$ (B) for group 1 and group 2 (children younger than 1 year). No statistical difference between the "eventually operated" and "never operated" children with p-values of 0.176, 0.345, 0.134, and 0.515 respectively. Note: divided into A and B owing to different scales.

Figure 4: A: Radar chart of mean vector measurements of 12 landmarks in millimetres for Group 1 (dashed line) and Group 4 (solid line) B: Bar chart in which the x-axis represents forehead landmarks, and the y-axis is difference in millimetres between the mean of vector measurements of Group 4 and Group 1.

Figure 5: bird-eye views of examples of the three types of forehead narrowing (top row), along with matching radar charts of the scans' vector measurements (bottom row). A: bifrontal narrowing ($APWR_1 < 0.90 < APWR_2$). B: Bitemporal narrowing ($APWR_2 < 0.90 < APWR_1$). C: Frontotemporal narrowing ($APWR_1$ and $APWR_2 < 0.90$)