The Jugular Foramen in Complex and Syndromic Craniosynostosis and Its Relationship to Raised Intracranial Pressure

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The Jugular Foramen in Complex and Syndromic Craniosynostosis and Its Relationship to Raised Intracranial Pressure

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BACKGROUND AND PURPOSE: Complex and syndromic craniosynostosis can be complicated by raised intracranial pressure (ICP), which in the absence of other identifiable origins, is probably caused by venous hypertension. Children with these conditions have been shown to have narrowing of the sigmoid sinus–jugular vein complex. Evidence of bony narrowing of the jugular foramina in children with complex or syndromic craniosynostosis and raised ICP compared with that in children with craniosynostosis without raised ICP would provide support for the theory that venous hypertension occurs in the former children.

METHODS: Measurements of the jugular foramina were obtained from reformatted helical CT scans obtained in 12 children with complex or syndromic craniosynostosis and raised ICP (group 1) and in two control groups of children with normal ICP. The first control group comprised 10 children with simple nonsyndromic synostosis of one or two sutures (group 2), and the second control group included nine children with complex or syndromic craniosynostosis (group 3).

RESULTS: Children with raised ICP had narrower jugular foramina than did the age-matched control subjects. For group 1, the mean diameter of jugular foramina was 6.5 mm; group 2, 11.5 mm ($P < .01$); and group 3, 10 mm ($P < .05$). No significant difference existed between the two control groups.

CONCLUSION: Significantly narrower jugular foramina in children with raised ICP is further evidence of the role of venous outflow obstruction and intracranial venous hypertension in the development of raised ICP in complex and syndromic craniosynostosis.
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without reference to clinical details at the time the data were
the image manipulation and measurements, in random order,
aforementioned criteria. But we were limited by the availability of patients who filled the
were age matched as closely as possible with the study group,
scans were used for comparative analysis. Both control groups
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included patients with simple, nonsyndromic synostosis of one
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synostosis (five with Apert, four with Pfeiffer, one with Crou-
zon, and one with Saethre-Chotzen syndrome) and one had
nonsyndromic complex craniosynostosis. Raised ICP was found
in 10 cases on the basis of monitoring ICP during a 24-hour
period by using a Camino fiber optic device (Camino Labora-
tories, San Diego, CA) placed in the subdural space with the
patient under general anesthesia. In the remaining two cases,
raised ICP was identified on the basis of clinical examination
(papilledema). No patient had active hydrocephalus (progres-
sive ventricular enlargement) at the time of the study.
Two control groups were drawn from children referred to
the Craniofacial Centre who had normal ICP. The first group
included patients with simple, nonsyndromic synostosis of one
or two sutures and no clinical evidence of raised ICP. CT data
were accessible for review in 10 suitable cases. Eight children
had unicoronal and two had bicoronal craniosynostosis (age
range, 2 months to 6 years; mean age, 2 years 5 months). The
second control group comprised children with complex or syn-
dromic craniosynostosis that had been shown by ICP monitor-
ing to have normal ICP. Nine children comprised this group;
five in the group had undergone CT twice. Eight children had
syndromic craniosynostosis (three with Apert, three with Crou-
zon, one with Apert-like, and one with Saethre-Chotzen syn-
drome) and one with nonsyndromic complex craniosynostosis
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were age matched as closely as possible with the study group,
but we were limited by the availability of patients who filled the
aforementioned criteria.
A single pediatric neuroradiologist (P.M.R.) undertook all
the image manipulation and measurements, in random order,
without reference to clinical details at the time the data were
acquired. Multiplanar reformatted images of the skull base
were created to allow measurement of the jugular foramina. A

Methods

Children referred to the Craniofacial Centre with complex
or syndromic craniosynostosis routinely undergo CT as part of
their diagnostic and preoperative assessment. Since 1996, im-
ages of the skull have been obtained by a helical technique on a
Somatom Plus 4 CT scanner (Siemens, Erlangen, Germany) with
2-mm collimation and a pitch of 1.5 through the skull base
and face. The vault is scanned using a pitch of 1 to avoid a step
artifact on the 3D reconstructed images.

For 12 of the patients with complex craniosynostosis and
raised ICP, who presented since this imaging protocol was
instituted, the imaging data sets were archived in a form acces-
sible for retrospective analysis of the skull base by means of
multiplanar reformatted images. These 12 children formed the
study group (age range, 2 months to 10 years 10 months; mean
age, 5 years 3 months). Eleven children had syndromic cranio-
synostosis (five with Apert, four with Pfeiffer, one with Crou-
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acquired. Multiplanar reformatted images of the skull base
were created to allow measurement of the jugular foramina. A

Results

Full data are presented in tabulated form (Tables 1–3). The combined mean diameter of the jugular
foramina for all the patients in each group was 6.5
mm in the study group (group 1), 11.5 mm in the
simple craniosynostosis control group (group 2), and
10 mm in the control group of patients with complex
or syndromic craniosynostosis but normal ICP (group
3). Significant differences existed between the study
group and each of the control groups (group 1 versus
group 2, $P < .01$; group 1 versus group 3, $P < .05$) (Figs 3 and 4).

Some discrepancy existed between the ages of the patients in the different groups, particularly between group 3 and the other two groups, and because it is possible (7, 16) that the pattern of bony abnormality can change with age, an attempt was made to age match subgroups so that more detailed comparisons could be made.

If only patients at or younger than 6 years were considered in the study group and group 2, inclusion of all except the oldest three patients in the study group and the whole of the control group was allowed. A significant difference in combined mean diameter of the jugular foramina was still noted between these subgroups (5 versus 11.5 mm; $P < .001$), as between the study group and the control group 3 (5 versus 9.5 mm; $P < .05$). Similarly, when comparing only children at or younger than 3 years, the differences between groups 1 and 2 (5.5 vs 10 mm; $P < .05$) and groups 1 and 3 (5.5 vs 10 mm; $P < .05$) were still significant.

The differences between the combined mean diameters in control groups 2 and 3 were not significant, either between the whole groups (11.5 versus 10 mm) or between the subgroups of subjects at or younger than 3 years (10.5 versus 10 mm) or 6 years (11.5 versus 9.5 mm).

Venous imaging was reviewed for patients 1, 6, and 12 of the study group. Patient 1 underwent angiography at 2 years old. The jugular bulbs were patent.

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**TABLE 1: Subjects (syndromic craniosynostosis with increased ICP)**

<table>
<thead>
<tr>
<th>No.</th>
<th>Age</th>
<th>Diagnosis</th>
<th>Jugular foramina (mm)</th>
<th>Combined (right plus left)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Right (mean)</td>
<td>Left (mean)</td>
</tr>
<tr>
<td>1</td>
<td>2 mo</td>
<td>Apert</td>
<td>1.9/3.2 (2.55)</td>
<td>2.0/3.1 (2.55)</td>
</tr>
<tr>
<td>2</td>
<td>1 yr 4 mo</td>
<td>Crouzon</td>
<td>2.1/2.4 (2.25)</td>
<td>2.8/2.5 (2.65)</td>
</tr>
<tr>
<td>3</td>
<td>1 yr 5 mo</td>
<td>Saethre-Chotzen</td>
<td>1.6/2.6 (2.1)</td>
<td>1.8/2.1 (1.95)</td>
</tr>
<tr>
<td>4</td>
<td>1 yr 6 mo</td>
<td>Pfeiffer</td>
<td>1.6/3.9 (2.75)</td>
<td>1.5/2.4 (1.95)</td>
</tr>
<tr>
<td>5</td>
<td>2 yr 10 mo</td>
<td>Apert</td>
<td>0.9/1.0 (0.95)</td>
<td>1.5/3.0 (2.25)</td>
</tr>
<tr>
<td>6</td>
<td>3 yr</td>
<td>Pfeiffer</td>
<td>5.7/6.2 (5.95)</td>
<td>1.8/2.4 (2.1)</td>
</tr>
<tr>
<td>7</td>
<td>3 yr</td>
<td>Pfeiffer</td>
<td>2.6/3.9 (3.25)</td>
<td>4.0/6.9 (5.45)</td>
</tr>
<tr>
<td>8</td>
<td>5 yr</td>
<td>Pfeiffer</td>
<td>0.8/1.5 (1.15)</td>
<td>2.5/2.7 (2.6)</td>
</tr>
<tr>
<td>9</td>
<td>5 yr</td>
<td>Pfeiffer</td>
<td>1.0/2.7 (1.85)</td>
<td>2.4/2.4 (2.4)</td>
</tr>
<tr>
<td>10</td>
<td>8 yr</td>
<td>Apert</td>
<td>4.7/3.3 (4.0)</td>
<td>4.0/5.3 (4.65)</td>
</tr>
<tr>
<td>11</td>
<td>9 yr 7 mo</td>
<td>Apert</td>
<td>1.3/3.8 (2.55)</td>
<td>4.6/4.0 (4.3)</td>
</tr>
<tr>
<td>12</td>
<td>10 yr 10 mo</td>
<td>Complex</td>
<td>4.9/12.9 (8.9)</td>
<td>4.0/7.3 (5.65)</td>
</tr>
</tbody>
</table>

**TABLE 2: Controls (Nonsyndromic)**

<table>
<thead>
<tr>
<th>No.</th>
<th>Age</th>
<th>Diagnosis</th>
<th>Jugular foramina (mm)</th>
<th>Combined (right plus left)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Right (mean)</td>
<td>Left (mean)</td>
</tr>
<tr>
<td>1</td>
<td>2 mo</td>
<td>Unicoronal</td>
<td>1.6/4.3 (2.95)</td>
<td>3.3/4.4 (3.85)</td>
</tr>
<tr>
<td>2</td>
<td>4 mo</td>
<td>Unicoronal</td>
<td>1.5/2.1 (1.8)</td>
<td>3.8/5.9 (4.85)</td>
</tr>
<tr>
<td>3</td>
<td>1 yr 2 mo</td>
<td>Unicoronal</td>
<td>2.9/5.4 (4.15)</td>
<td>4.5/8.2 (6.35)</td>
</tr>
<tr>
<td>4</td>
<td>1 yr 2 mo</td>
<td>Unicoronal</td>
<td>6.0/8.1 (7.05)</td>
<td>3.3/5.6 (4.45)</td>
</tr>
<tr>
<td>5</td>
<td>1 yr 5 mo</td>
<td>Unicoronal</td>
<td>5.2/9.9 (7.55)</td>
<td>4.7/6.8 (5.75)</td>
</tr>
<tr>
<td>6</td>
<td>1 yr 8 mo</td>
<td>Unicoronal</td>
<td>2.2/2.2 (2.2)</td>
<td>3.9/7.9 (5.9)</td>
</tr>
<tr>
<td>7</td>
<td>2 yr 2 mo</td>
<td>Unicoronal</td>
<td>5.3/5.7 (5.5)</td>
<td>4.6/13.5 (9.05)</td>
</tr>
<tr>
<td>8</td>
<td>3 yr 5 mo</td>
<td>Unicoronal</td>
<td>5.2/7.8 (6.5)</td>
<td>7.7/8.9 (8.4)</td>
</tr>
<tr>
<td>9</td>
<td>5 yr 3 mo</td>
<td>Bicoronal</td>
<td>2.8/7.8 (5.3)</td>
<td>4.2/13.6 (8.9)</td>
</tr>
<tr>
<td>10</td>
<td>6 yr</td>
<td>Bicoronal</td>
<td>3.8/6.7 (5.25)</td>
<td>10.2/9.2 (9.7)</td>
</tr>
</tbody>
</table>

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**Figs 2.** Parasagittal reformatted image (left) produced from an axial CT scan (right). These show measurements of the right jugular foramen in two orthogonal planes (control group 2, patient 9).
Mastoid emissary veins were seen bilaterally. Patient 6 also underwent angiography at 2 years old; a patent right jugular bulb but an occluded left jugular bulb—transosseous segment and extensive collateral emissary vessels were discovered. Patient 12 underwent angiography at 9 years old; jugular bulbs were patent, and stylomastoid emissary veins and transosseous drainage from the sagittal sinus was evident.

### Discussion

In our study, children with complex or syndromic craniosynostosis and raised ICP had significantly narrower jugular foramina than did children with simple craniosynostosis and normal ICP. This might have been predicted, because children with complex craniosynostosis inevitably have severe abnormalities of the skull.
had both developed abnormally large additional emissary veins, suggesting inadequacy of normal venous drainage pathways. The third patient (patient 6) had unilateral jugular atresia, and again, extensive collateralization. In this case, a greater discrepancy existed than in the other two cases between the size of the jugular foramen on the side of the atretic vein compared with that of patients in the simple craniosynososis control group.

Of note is that although the second, complex, control group was found to have significantly larger jugular foramina than those in the study group, in individual cases, some foramina were also rather narrow. This suggests that in some cases, it is the capacity to develop collateral venous drainage rather than the patency of the usual routes, such as the jugular foramina, that determines whether raised ICP occurs. This is consistent with the finding of enlarged emissary foramina in similar patients in the aforementioned study (13). Considering that intracranial venous drainage is usually transmitted through various portals in the skull base, the development of dilated collateral veins despite angiographically normal jugular bulbs and transosseous jugular segments can be explained. Complex craniosynososis inevitably involves distortion of the skull base and therefore interruption of at least some of the numerous normal emissary routes of venous drainage, even if the jugular foramina are not severely affected. This might explain why emissary vessel enlargement is so variable.

However, our results also imply that jugular venous outflow obstruction has a major role in the genesis of raised ICP. The jugular bulb develops after birth (19), and in early infancy, alternative emissary veins have a more important functional role than after establishment of a more adult pattern of jugular venous drainage. Our individual jugular foramen measurements show a greater discrepancy between the study and control groups for children older than 1 year, when this is likely to be more hemodynamically significant, than in the individual patients examined during the 1st year of life. This correlates with the occurrence of raised ICP in children with complex craniosynososis, most commonly during the 2nd year of life. The previously mentioned tendency toward normalization of ICP at approximately 6 years of age (7) may be due to maturation of collateral emissary veins.

Some early studies (including those in animal subjects) seemed to show an inconsistent relationship between jugular foramen narrowing, venous hypertension, and raised intracranial pressure and also addressed the question of whether intracranial venous hypertension is a cause or effect of raised ICP. Steinbok et al (10) undertook a careful review of this work, and they argued that more recent and definitive studies favored the view that jugular foramen stenosis is a cause of venous outflow obstruction, and therefore, intracranial venous hypertension and hydrocephalus. They performed experiments in children with achondroplasia that supported this theory. This position has also been adopted by others (11, 12, 20), including
Sainte-Rose et al (8), whose work very strongly supports the notion that intracranial venous hypertension in the setting of foraminal stenosis is not secondary to raised intraventricular pressure and may be relieved by venous bypass. The latter study included cases of achondroplasia and also craniosynostosis.

Our control group of children with complex craniosynostosis included five patients who had undergone CT twice, at intervals of between 7 and 22 months. In two cases, the foramina were slightly larger on the second scan; in two, the combined mean diameter was the same; and in one, the combined mean diameter was fractionally less. Whether this represents a genuine increase in the severity of stenosis or simply reflects the tolerance limit of our measuring technique cannot be determined on the basis of a single case. The normal ranges for a jugular foramen cross-sectional area from the aforementioned study (13) do show a gradual increase in the predicted value of the mean area of the foramina between the ages of 1 month and 16 years. However, the range of measurements for each age group is so wide that normal children at 1 year and 16 years of age could have the same size foramina. Therefore, we cannot draw any conclusions from our limited serial data.

MR venography has been used to study 17 patients with complex craniosynostosis (21), ranging from 4 months to 34 years of age (mean age, 7.3 years). Jugular bulb obstruction was found in 12 patients, but a variable relationship with tonsillar herniation and hydrocephalus existed, and no correlation was made with ICP measurements. Stenosis of the jugular bulbs was not consistently related to osseous narrowing of the jugular foramina on CT scans. This finding may be important, because it indicates that in selected cases, soft-tissue hypertrophy or encroachment may be the cause of jugular bulb stenosis, which might be amenable to endovascular dilation or stent placement rather than surgical foraminoplasty.

Quantitation of dural venous sinus flow and velocity is also possible with MR venography by using a cine phase contrast technique. Superior sagittal sinus blood flow was studied by using this technique in normal children and in children with achondroplasia or obstructive hydrocephalus (22). Flow was shown to increase in normal children during the first 6 to 8 years of life. Reduced superior sagittal sinus flow was observed in the achondroplastic children but not in those with obstructive hydrocephalus, although the number of children studied was too small to achieve statistical significance. Nonetheless, noninvasive quantification of intracranial venous hemodynamics would be a useful adjunct to the imaging assessment of complex craniosynostosis and achondroplasia, particularly in patients who are likely to develop progressive venous outflow obstruction.

Achondroplasia presents a precedent for the relationship between raised ICP and jugular foramen stenosis and its treatment; it is also a disorder that is mediated by a fibroblast growth factor receptor mutation (23). Like syndromic craniosynostosis, it is associated with hydrocephalus and raised ICP, with constriction of the internal jugular veins in the foramina narrowed by early closure of skull base syndromoses (10). In children with achondroplasia and craniosynostosis, invasive monitoring has been used to show persistently elevated superior sagittal sinus venous pressure despite decompression of the ventricles and lowering of ICP by removal of CSF via a ventricular drain (8). The children in that series also had venous stenoses and a pressure gradient between the superior sagittal sinus and the internal jugular veins, with development of a collateral venous circulation. Lateral sinus-to-jugular vein bypass operations were performed in three patients. Two patients also required insertion of a ventriculoperitoneal shunt to control ICP, but in the third, a reduction in ICP was achieved with the bypass procedure alone. Relief of raised ICP by surgical decompression of jugular foramen stenosis has also been reported in association with achondroplasia (9).

Conclusion

We have shown that in complex and syndromic craniosynostosis, the jugular foramina are significantly narrower in patients with raised ICP than in those with normal ICP. This adds to a growing body of published evidence that intracranial venous hypertension is an important factor in the development of raised ICP and hydrocephalus in these children. Venography should form part of the routine MR imaging protocol for diagnostic assessment of children with complex and syndromic craniosynostosis. Quantification of venous hemodynamics may also have a role, allowing more accurate, noninvasive monitoring of change at follow-up studies. Future management strategies in appropriate patients with raised ICP should be directed at alleviating venous outflow obstruction, either by surgical or endovascular techniques. Prophylactic intervention may also play a role in children who have normal ICP but radiologic evidence of venous outflow obstruction if it becomes possible to reliably identify those patients who are destined to develop raised ICP and the related neurodevelopmental sequelae.

References

6. Thompson DN, Harkness W, Jones BM, Hayward RD. Aetiology of herniation of the hindbrain in craniosynostosis: An investigation incorporating intracranial pressure monitoring and magnetic res-