

# Is There a Causal Relationship Between Open Spinal Dysraphism and Chiari II Deformity?: A Study Using in Utero Magnetic Resonance Imaging of the Fetus

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**BACKGROUND:** Chiari II deformity is associated with open spinal dysraphism. A causal relationship has been proposed by McLone and Knepper. This article evaluates that hypothesis.

**OBJECTIVE:** To establish the frequency of Chiari II deformity in fetuses with open spinal dysraphism, assess whether meningocele sac neck area and volume influence the severity of posterior fossa changes, and assess whether the severity of associated findings (ventriculomegaly, amount of extracerebral CSF) are associated with Chiari II deformity.

**METHODS:** Sixty-five fetuses with open spinal dysraphism were compared with gestationally aged matched “normal” fetuses on ultrafast MR images. Cerebellar vermis and bony posterior fossa surface area were measured on midline sagittal images. Hindbrain herniation was noted if present. In the open spinal dysraphic group, sac neck area and volume were measured. Ventriculomegaly was assessed by linear measurement of the trigone of the lateral ventricle and extracerebral CSF depth was measured maximally over the lateral surface of the cerebral hemispheres.

**RESULTS:** Fifteen of 65 fetuses with open spinal dysraphism did not have Chiari II deformity. Neck area and volume of the sac did not correlate with the presence of Chiari II deformity or reduction in bony posterior fossa size.

**CONCLUSION:** A relatively high proportion of fetuses with open spinal dysraphism do not have Chiari II deformity in utero. There is a lack of correlation between indicators of spinal dysraphism severity and the extent of the posterior fossa abnormality. This raises some interesting questions about the causality of the Chiari II deformity.

**KEY WORDS:** Chiari II, Fetal magnetic resonance, Myelomeningocele, Spinal dysraphism

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The mechanism by which the normal bony posterior fossa develops is not known with certainty, but one widely held theory suggests that hydrostatic pressure transmitted through the cerebrospinal fluid (CSF) is an important factor for normal development of the bony posterior fossa.<sup>1</sup> That theory proposed by McLone and Knepper suggests there is an increase in CSF pressure, specifically in the posterior fossa, during the first trimester of pregnancy brought about by a physiological

block to CSF in the spinal compartment. The increased pressure induces growth in the bony confines of the posterior fossa, which would otherwise lag behind growth of the rest of the developing calvarium.

Open spinal dysraphism in the lower spine is thought to be due to the failure of primary neurulation and, as a result, the neural placode is exposed and CSF is lost externally. The McLone and Knepper hypothesis proposes that this spinal malformation prevents normal transient occlusion of the primitive central canal of the spinal cord and the buildup of hydrostatic pressure in the rhombencephalon. This subsequently produces a posterior fossa that is too small and hence explains the association of open

**ABBREVIATIONS:** **iuMR**, in utero magnetic resonance; **MMC**, myelomeningocele; **SSFSE**, single-shot fast spin echo

spinal dysraphism and the Chiari II deformity.<sup>1</sup> Open spinal dysraphism has 4 forms: myelomeningocele (MMC), myelocele, hemimyelomeningocele, and hemimyelocele, MMC being by far the most common.<sup>2</sup> It is widely accepted in the literature that there is a high association between open spinal dysraphism and Chiari II deformity,<sup>3</sup> with some authors claiming that the association is constant.<sup>4</sup> The Chiari II deformity is a complex of abnormalities involving both infra- and supratentorial compartments, but the main features are small bony posterior fossa with hindbrain herniation both caudally through the foramen magnum and cranially through the tentorial incisura.<sup>3,5,6</sup>

A more recently recognized finding is the paucity of extraventricular CSF within the posterior fossa and over the cerebral hemispheres, which has been well demonstrated on in utero magnetic resonance (iuMR) imaging.<sup>7</sup> The Chiari II deformity can occasionally be found in fetuses with closed spinal dysraphism (posterior meningocele and myelocystocele), but this is unusual. In such cases, it is proposed that there is sufficient CSF loss into the closed defect to produce intracranial hypotension with resultant Chiari II deformity development.<sup>4</sup>

We have performed iuMR at our institution for more than 10 years and have seen several fetuses with apparent open spinal dysraphism, but with no obvious Chiari II deformity (that is, no hindbrain herniation). In this article we review the first 65 cases of open spinal dysraphism shown on iuMR with the aim of testing the following hypotheses arising from McLone and Knepper's theory:

All fetuses with open spinal dysraphism will have Chiari II deformity.

The size and apparent growth rate of the cerebellar vermis in fetuses with open spinal dysraphism is the same as in controls.

The size and apparent growth rate of the bony posterior fossa in fetuses with spinal dysraphism are reduced in comparison with controls.

There is a positive correlation between the indicators of severity of the spinal malformation and the reduction in posterior fossa size.

## PATIENTS AND METHODS

### Patient Details

The study included all fetuses referred from antenatal ultrasonography with lumbosacral spinal malformations confirmed as open spinal dysraphism by iuMR at our institution between 2000 and 2007. The study was approved by the local ethics committee, and informed written consent was obtained from all of the women.

Sixty-five fetuses with open lumbosacral dysraphism had iuMR between 18 and 34 weeks gestation (calculated from the last menstrual period). The MR diagnosis of open spinal dysraphism was confirmed independently by 2 radiologists experienced in fetal MR, using the presence of visualized neural tissue in a non-skin-covered sac as the iuMR signs to confirm an open dysraphism. In addition, 65 fetuses with normal brains and spines, matched for gestational age to the open spinal dysraphism group, were also included in the study. Most of those fetuses underwent iuMR because of a family history of a possible brain or spine

abnormality but were found to be normal. The normal fetuses were selected chronologically and consecutively from 2000 to 2007 (and were interpreted as normal by the same radiologists who reported the abnormal iuMR scans).

### In Utero MR Imaging Technique

The iuMR imaging was performed on a 1.5T superconducting system (Eclipse or Infinion, Philips Medical Systems, Cleveland, Ohio). A flexible, phased-array surface coil was placed over the lower abdomen of the woman. Imaging consisted of a T2-weighted (TR 20 000–32 000, TE 75) single-shot fast spin echo (SSFSE) sequence in 3 orthogonal planes (5 mm and 3 mm slice thickness, Echo Train Length 132, field of view 20 × 25 cm, matrix size 256 × 256) of the brain and spine. All data sets were analyzed on the proprietary workstation.

### Image Analysis

All of the studies were analyzed on the MR system's proprietary software and each observation was made by averaging 6 measurements (3 each, which were done by 2 observers).

Intra- and interuser variability of cerebellar vermis surface area and bony posterior fossa surface area were assessed by repeated measurements over a week apart, on consecutive cases, by 2 observers working independently.

### Spine

For the purpose of this study, the neck of the sac of the open spinal dysraphism was defined as the defect at the skin surface. Maximum craniocaudal and transverse diameters of the neck were measured on sagittal and axial spinal images (Figure 1A). The area of the neck of the sac was then estimated as the area of an ellipse. We found that this method of calculating neck area was more reproducible than a single freehand coronal measurement. The volume of the open spinal sac was estimated by measuring maximum sac diameters in 3 orthogonal planes on sagittal and axial spinal images (Figure 1B). No measurements were made in the spine of the control group. The segmental level of the open spinal defect was estimated.

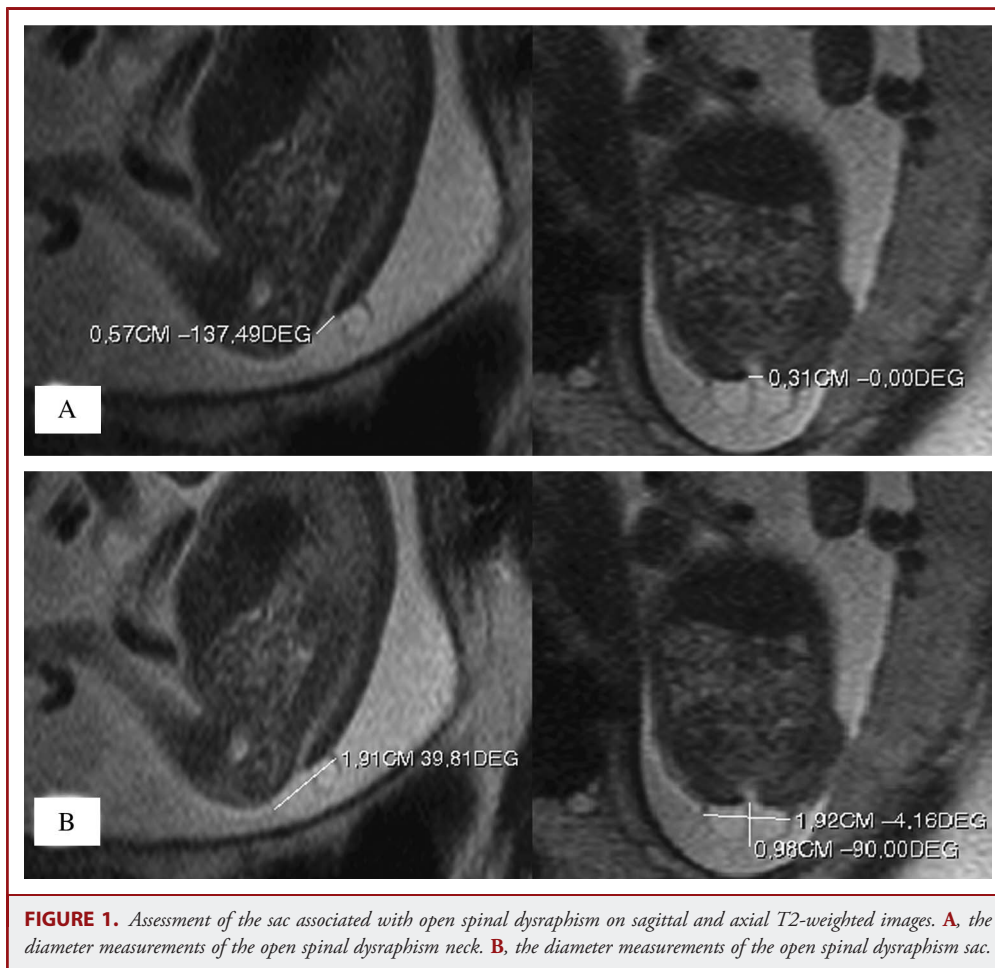
### Cranium

The presence or absence of hindbrain herniation was judged on sagittal imaging of the cranium and defined by any part of the cerebellum lying below a line joining the opisthion and the basion (Figure 2). The maximum transverse diameter of the trigone of the lateral ventricles was measured on the axial images of the brain at the level of the thalamus, cavum septum pellucidum, and sylvian fissure (Figure 3A). The maximum depth of CSF was measured perpendicular to the lateral surface of the cerebral hemisphere above the level of the lateral ventricles on axial images (Figure 3B).

A freehand line was used to outline the cerebellar vermis on the midline sagittal brain image and calculate the area (Figures 2A and 2B). The surface area of the bony posterior fossa was estimated by drawing 5 straight lines around its perimeter on the midline sagittal image of the brain, and the surface area was calculated. The lines connected the torcular to the opisthion, the opisthion to the basion, the basion to the dorsum sellae, and the dorsum sellae to the anterior aspect of a line along the superior aspect of the tentorium (Figures 2C and 2D).

### Statistical Analysis

The area of the neck of the sac and the volume of the sac was correlated with the surface area of the bony posterior fossa, and Pearson coefficients



were calculated. The area of the neck of the sac in fetuses with and without hindbrain herniation were compared by the use of 2-tailed paired  $t$  test analysis at a 5% significance level. The volume of the sac did not conform to a normal distribution, and the Wilcoxon signed-rank test was used to compare fetuses with and without hindbrain herniation matched for gestational age.

The maximum transverse diameter of the trigone of the lateral ventricles and the maximum depth of CSF in the control group were compared with fetuses with an open spinal dysraphism by the use of 2-tailed paired  $t$  test analysis at a 5% significance level.

The estimated surface areas of bony posterior fossa and the cerebellar vermis were plotted against gestational age in cases of open spinal dysraphism and controls. Linear regression was performed for each data set ( $y = mx + c$ ) by the use of the least-squares method, and Pearson coefficients were calculated to assess correlation. The regression coefficient of each line (gradient  $m$ ) was used to calculate the "apparent" growth rate. We accept that there are errors in this method of estimating growth rate, because these are not longitudinal data (repeated measurements on the same fetus at different gestations), but pooled data from several fetuses of different gestation, each measured once. This method has been used and published previously in postmortem studies of the fetus.<sup>8</sup> We tested our original hypotheses concerning the cerebellar

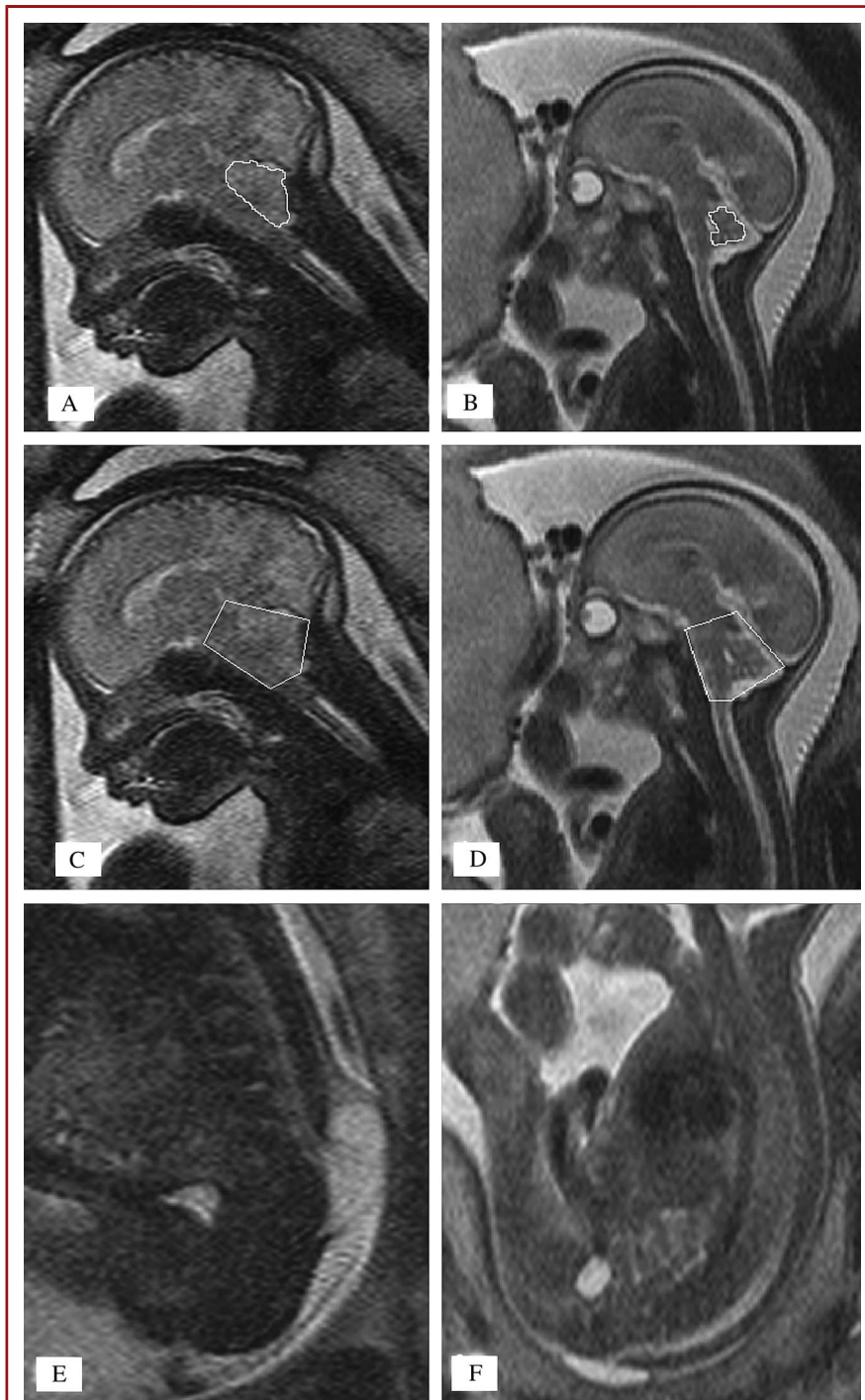
vermis surface area and bony posterior fossa surface area by using a 2-tailed, paired  $t$  test analysis at a 5% significance level.

## RESULTS

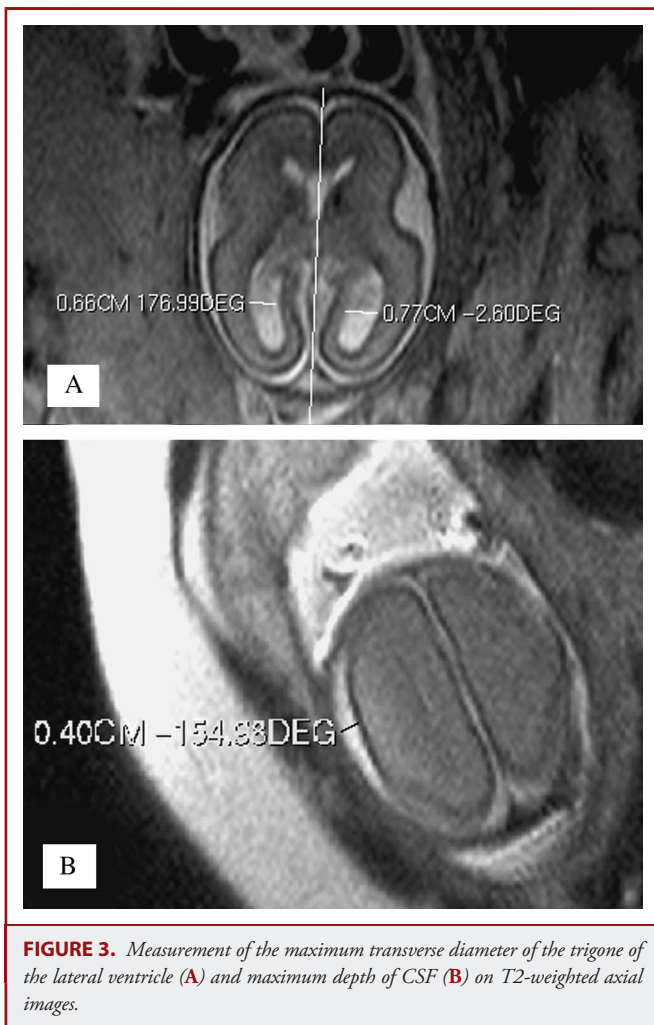
Sixty-four of 65 of the fetuses with open spinal dysraphism had a myelomeningocele, and 1 of 65 had a myelocele. For convenience, we use "MMC" to cover all cases of open spinal dysraphic spinal abnormalities from now on. As described previously, there was good matching of gestational age between the MMC and control group. In addition, the median gestational age of fetuses with MMC and Chiari II deformity was not significantly different from the gestational age of the group with MMC but no Chiari II deformity (22 weeks [range, 18-32] and 22 weeks [range, 18-34 weeks], respectively).

### Spinal Findings

MMC neck area was plotted against bony posterior fossa area (Figure 4A) for fetuses with and without Chiari II deformity. There was no correlation in either group with Pearson coefficients



**FIGURE 2.** Assessment of the posterior fossa and contents on midline T2-weighted sagittal images of the brain. **A**, freehand line drawn around the cerebellar vermis in a fetus with hindbrain herniation. **B**, freehand line drawn around the cerebellar vermis in a fetus without hindbrain herniation. **C**, 5 straight lines used to estimate the bony posterior fossa surface area in a fetus with hindbrain herniation. **D**, 5 straight lines used to estimate the bony posterior fossa surface area in a fetus without hindbrain herniation. **E**, sagittal image of the fetus shown in **A** and **C**, demonstrating the open spinal defect. **F**, sagittal image of the fetus shown in **B** and **D**, demonstrating the open spinal defect.

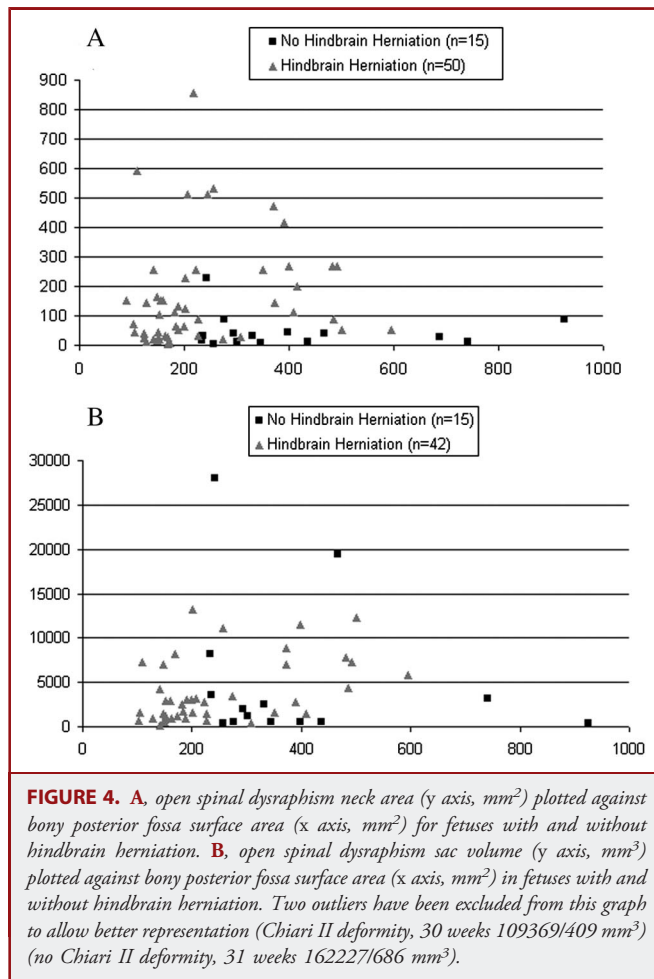


**FIGURE 3.** Measurement of the maximum transverse diameter of the trigone of the lateral ventricle (A) and maximum depth of CSF (B) on T2-weighted axial images.

close to zero (0.16 for Chiari II group and 0.06 for the no Chiari II group). There was no significant difference in neck area in fetuses with and without Chiari II deformity ( $P = .47$ ) with the use of the paired  $t$  test analysis.

It was not possible to measure sac volume diameters in 8 fetuses with Chiari II (1 with myelocoele and 7 with MMC), because the sac was not visualized in its entirety. For the other 57 cases, sac volume was plotted against bony posterior fossa area (Figure 4B) for fetuses with and without Chiari II deformity. Sac volumes did not show a correlation with bony posterior fossa area with Pearson coefficients of 0.28 for the Chiari II group and 0.32 for the group without Chiari II. There was no difference in sac volume between fetuses with MMC and Chiari II deformity and those without Chiari II deformity ( $z$  score = 1.25, which is not significant at the 5% level [critical  $z = 1.96$ ]).

The segmental level of the open spinal defect was estimated and categorized as high lumbar (L2 or above), low lumbar (L3 and L4), or lumbosacral (L5 or below). Nineteen percent (3/16) of fetuses with a high lumbar defect, 11% (3/27) of fetuses with a low lumbar



**FIGURE 4.** A, open spinal dysraphism neck area (y axis,  $mm^2$ ) plotted against bony posterior fossa surface area (x axis,  $mm^2$ ) for fetuses with and without hindbrain herniation. B, open spinal dysraphism sac volume (y axis,  $mm^3$ ) plotted against bony posterior fossa surface area (x axis,  $mm^2$ ) in fetuses with and without hindbrain herniation. Two outliers have been excluded from this graph to allow better representation (Chiari II deformity, 30 weeks 109369/409  $mm^3$ ) (no Chiari II deformity, 31 weeks 162227/686  $mm^3$ ).

defect, and 41% (9/22) of fetuses with a lumbosacral defect did not have a Chiari II deformity.

### Intracranial Findings

Fifteen of 65 (23%) of the fetuses with MMC did not have hindbrain herniation with the use of the criteria given above (now defined as Chiari II deformity). By definition, none of the “control” fetuses had hindbrain herniation.

It is widely accepted that ventriculomegaly tends to become more severe as pregnancy progresses in fetuses with Chiari II deformities, and, for that reason, we split the group into second and third trimester fetuses when analyzing the trigone measurements and CSF depth. Our referral patterns result in a clear demarcation between 18- to 24-week and 29- to 34-week groups, with no referrals between 25 and 28 weeks gestational age. The mean transverse diameters of the trigones of the lateral ventricles (Table 1) for fetuses with Chiari II deformity were statistically larger than those in controls in both gestational age groups. The trigones were statistically larger in the third-trimester group in comparison with the second-trimester group for fetuses with

**TABLE 1. Summaries of the Size of the Trigones of the Lateral Ventricles and Depth of CSF Overlying the Cerebral Hemispheres in Control and in Fetuses With Open Dysraphic Abnormalities and Different Gestational Ages<sup>a</sup>**

		Control Cases	All MMC Cases	MMC and Chiari II	MMC but No Chiari II
<b>Lateral ventricles</b>					
18- to 24-wk group	N	48	48	37	11
	Mean, mm	6.8	11.6 <sup>b</sup>	12.3 <sup>b</sup>	9.3 <sup>b</sup>
	SD, mm	1.2	3.1	3.1	1.6
	Range, mm	3-9	6-18	7-18	6-12
	% >10 mm	0%	56%	68%	18%
29- to 34-wk group	n	17	17	13	4
	Mean, mm	5.4	15.8 <sup>b</sup>	17.9 <sup>b</sup>	9.0 ns
	SD, mm	1.8	7.5	7.4	1.8
	Range, mm	2-9	7-32	10-32	7-11
	% >10 mm	0%	71%	85%	25%
<b>Depth of CSF overlying the cerebral hemispheres</b>					
18- to 24-wk group	N	48	48	37	11
	Mean, mm	4.6	1.4 <sup>b</sup>	0.3 <sup>b</sup>	5.1 ns
	SD, mm	1.2	2.9	0.7	4.3
	Range, mm	2-7	0-15	0-0.3	0-15
	% <1 mm	0%	69%	100%	9%
29- to 34-wk group	N	17	17	13	4
	Mean, mm	7	2.8 <sup>c</sup>	1.1 <sup>b</sup>	8.5 ns
	SD, mm	1.9	3.8	1.4	3.7
	Range, mm	5-11	0-9	0-4	3-9
	% <1 mm	0%	41%	54%	0%

<sup>a</sup>The statistical information for each null hypothesis test is at the 5% significance level (the control group has been compared with the other columns in each case). ns, not statistically different.

<sup>b</sup>Statistically significant at <.001.

<sup>c</sup>Statistically significant at <.01.

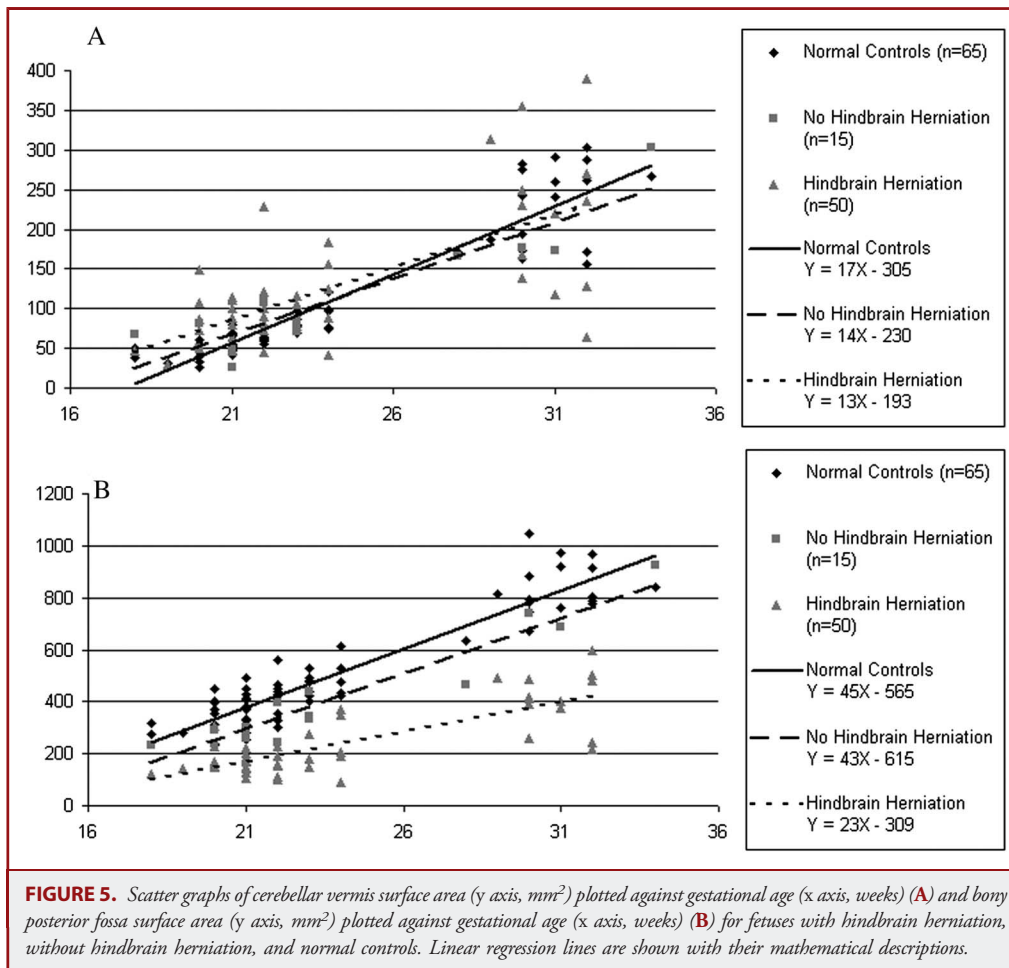
Chiari II deformity. There was no significant difference in trigone size in the third trimester in the MMC but no Chiari II deformity group, compared with controls, although the number of cases available for study was very small (4).

The presence or absence of a Chiari II deformity had statistically significant effects on trigone size in the 18- to 24-week group. In cases with MMC and Chiari II deformity, the mean measurement was  $12.3 \pm 3.1$  mm, and with MMC but no Chiari II deformity the mean was  $9.3 \pm 1.6$ , which reached significance within the <.05 level. There were too few cases in the MMC but no Chiari II deformity group at 29 to 34 weeks to make formal assessments, but similar trends were identified. With the use of 10 mm as the cut point for describing ventriculomegaly, 36 of 50 (72%) of fetuses with MMC and Chiari II deformity had ventriculomegaly, whereas this occurred in only 3 of 15 (33%) of fetuses with MMC with no Chiari II deformity.

The mean CSF depth was significantly reduced in the whole group of fetuses with MMC compared with controls in both the 18- to 24-week and the 29- to 34-week groups (Table 1). That finding retained statistical significance when the MMC and Chiari II deformity group was analyzed separately. There was no effective CSF depth measurable in the 18- to 24-week fetuses of that group. The CSF depth in the MMC with no Chiari II deformity group was not statistically different from controls.

Two-tailed paired *t* test showed no significant difference in cerebellar vermis surface area between fetuses with and without Chiari II deformity and controls ( $P > .08$ ). Pearson coefficients for the linear regression lines of cerebellar vermis area were 0.74 and 0.98 for fetuses with MMC and controls, respectively. The MMC group was separated into fetuses with and without Chiari II deformity (Figure 5A). The Pearson coefficients for the linear regression lines were 0.70 and 0.91 for fetuses with and without Chiari II deformity, respectively. The apparent growth rates of the cerebellar vermis area were similar in all 3 groups ranging from 13 to 17 mm<sup>2</sup> per week.

The area of the bony posterior fossa was significantly reduced in the whole group of fetuses with MMC in comparison with controls at all gestational ages ( $P < .001$ ). Pearson coefficients for the linear regression lines were 0.73 and 0.94 for fetuses with open spinal dysraphism and normal controls, respectively. The data for fetuses with and without Chiari II deformity were compared with the control group separately (Figure 5B). Fetuses in the control group had the largest posterior fossae, and the smallest were found in fetuses with MMC and Chiari II. Values for fetuses with MMC but no Chiari II deformity were in between those 2 groups. The differences in area of the bony posterior fossa between all 3 groups reached statistical significance ( $P < .01$ ). Pearson coefficients for the linear regression lines were 0.78 and



0.96 for fetuses with and without Chiari II deformity, respectively. Bony posterior fossa surface area estimated growth rates were calculated at 23, 43, and 45 mm<sup>2</sup> per week for fetuses with MMC and Chiari II, fetuses with MMC but without Chiari II, and controls, respectively.

There was no significant difference in intra- and interuser variability in measurement of cerebellar vermis and bony posterior fossa surface areas. Values for intrauser variability for cerebellar vermis surface area were  $T(19) = 0.62$  (critical  $t = 2.09$ ) with  $P(T \leq t)$  of .54 (mean, 1.2; standard deviation, 8.65; confidence intervals [95%] 3.79, for the differences between the observations), and for bony posterior fossa surface area  $T(19) = 1.33$  (critical  $t = 2.09$ ) with  $P(T \leq t)$  of .20 (mean, 7.9; standard deviation, 26.52; confidence intervals [95%] 11.62, for the differences between the observations). Values for interuser variability for cerebellar vermis surface area were  $T(19) = 0.24$  (critical  $t = 2.09$ ) with  $P(T \leq t)$  of .81 (mean, 44.95; standard deviation, 58.51; confidence intervals [95%] 25.64, for the differences between the observations) and for bony posterior fossa surface area  $T(19) = 2.08$  (critical  $t = 2.09$ ) with  $P(T \leq t)$  of 0.051 (mean, -13.15; standard deviation,

28.26; confidence intervals [95%] 12.39, for the differences between the observations).

## DISCUSSION

iuMR is proving to be a reliable method of imaging spine and brain pathology in the developing fetus with measurable improvements in diagnostic accuracy when incorporated into the care pathway of pregnant women.<sup>7,9,10</sup> iuMR imaging provides excellent contrast resolution, which, in many situations, compensates for the lower spatial resolution of the ultrafast sequences compared with ultrasonography. The improvements in diagnostic accuracy are mainly due to correctly classifying the neural components of developmental abnormalities, but, conversely, there is relatively poor bone detail obtained from the spine by using SSFSEs. It has been shown, for example, that the level of a spinal abnormality with the use of iuMR imaging can be up to 2 segments out in 20% of cases.<sup>11</sup>

For the study arm of this project, we included fetuses whose iuMR showed an open dysraphic abnormality of the lumbar

and/or sacral spine as agreed upon by 2 radiologists experienced in imaging of the fetal central nervous system. The majority of those were MMC, and the imaging findings used to support that diagnosis were a non-skin-covered sac with neural elements seen within the sac. We will discuss the appropriateness of this approach below in the absence of a true reference standard. The most important finding of the study was the absence of Chiari II deformity (as indicated by lack of hindbrain herniation) in more than 20% of the cases with MMC. This is a controversial finding, because most textbooks describe an "invariable" association that, for many authorities, implies greater than 98%. Our observation, therefore, requires close scrutiny.

There are several reasons why the 20% rate of MMC cases with no Chiari II deformity in our study might arise from methodological errors. First, it is possible that hindbrain herniation does not occur until late in pregnancy or after delivery, in some cases. The rate of CSF loss through the open spinal defect could influence the severity of the posterior fossa malformation, but we had no means of quantifying CSF loss in utero. It is also possible that fetuses with MMC but without Chiari II deformity have a higher risk of spontaneous abortion, but there is no direct evidence to support either of those suggestions. It is more likely that classifications of the spinal malformations made on iuMR studies were incorrect. The abnormality that is most likely to have caused diagnostic confusion is a lumbrosacral meningocele, classified as "closed" spinal abnormalities and not thought to be associated with either Chiari II or with other intracranial abnormalities. The problem of misclassification could have been circumnavigated if "reference standard" diagnoses were available from either postmortem studies from terminated pregnancies or postnatal imaging from delivered infants. An unavoidable failing of our article is that reference standard data were not available in a large majority of cases. Most fetal MMC cases referred to us do not go on to delivery (current rate is less than 40%). In the vast majority of cases, no posttermination diagnostic procedure was performed on the basis of parental wishes, so only external examinations were made. This can (and did) confirm the presence of a sac in all cases but not its contents, which is required to differentiate between MMC and meningocele with confidence. We have previously shown good correlation between iuMR and pathology findings in earlier studies of brain and spine abnormalities, but these were not available for the majority of cases in this study.<sup>7</sup>

How could such errors in diagnosis on iuMR be made? The most reliable finding of MMC on iuMR is demonstration of internal structures within the sac, representing the placode and associated neural elements. It is possible that artifacts within the sac (perhaps arising from CSF flow in the sac) could cause diagnostic confusion. "Flow" artifacts are reasonably common on the axial SSFSE imaging in our experience; therefore, it was important to redemonstrate the placode/neural elements within a sac in another plane. In our study, this was done on the sagittal images in all cases. Notwithstanding the lack of reference standard data in our study, there is supportive evidence that the "MMC without Chiari II" group did indeed have open dysraphic spinal

abnormalities, at least in a high proportion of cases, and we will now review that circumstantial evidence.

The MMC without Chiari II group had intracranial findings similar to those associated with the Chiari II deformity other than hindbrain herniation in a high proportion of cases. Ventriculomegaly is known to develop in the majority of cases of Chiari II deformity postnatally and is thought to be due to hydrocephalus in most cases. It is also common in fetuses with MMC and Chiari II deformity, and there is no doubt that this is a dynamic process, ie, the severity tends to increase during pregnancy, as confirmed by the data in our study. A trigone measurement of 10 mm or greater at any stage of pregnancy is taken to be abnormal on antenatal screening and in our MMC and Chiari II deformity group ventriculomegaly of some severity was found in the majority of cases (68% in the 18- to 24-week group and 85% in the 29- to 34-week group). By definition, none of the control group of fetuses had trigone measurements of greater than 9 mm at any gestational age. Trigone measurements of 10 mm or greater were found in a small but statistically significant number of cases of MMC without Chiari II deformity in the 18- to 24-week group (18%), rising to 25% of the 29- to 34-week group (this did not reach statistical significance probably because of the small numbers in this group). These intracranial findings would not be expected in cases of closed spinal dysraphism such as meningoceles.

Reduction of CSF over the cerebral hemispheres is also a recognized finding associated with MMC on iuMR, and in this study we attempted to quantify the finding.<sup>7</sup> In control cases the mean CSF depth was 4.6 mm at 18 to 24 weeks and 7.0 mm at 29 to 34 weeks gestational age. These were significantly different from the fetuses with MMC and Chiari II deformity in which the CSF depth was less than 1 mm in all of the 18- to 24-week fetuses and 54% of the 29- to 34-week group. The maximum CSF depth in the MMC without Chiari II deformity was not significantly different from controls, although 1 fetus had a nonmeasurable CSF depth.

The sine qua non of Chiari II deformity, however, is reduced volume of the bony posterior fossa, and this is thought to give rise to the majority of the postnatal imaging findings such as hindbrain herniation, towering midbrain, fused colliculi, large foramen magnum, and scalloping of the posterior aspects of the petrous temporal bones. It would have been desirable to calculate the volume of the bony posterior fossa in our study rather than the mid sagittal area. This was not possible in our study, however, because of the long acquisition times of the volume data sets that would be required, although this may be possible in the future. It would have been inaccurate to calculate volumes from 3- or 5-mm-thick SSFSE images, and, in contrast, the area measurements that were made can be made quickly and with reasonable reproducibility.

Bony posterior fossa surface area was found to be statistically significantly smaller in fetuses with MMC and Chiari II deformity in comparison with control fetuses, as expected. Not only were they smaller at each gestational age studied, but the apparent growth rates were lower as well (by approximately 50%), resulting



in larger deviations from control values as pregnancy progressed. The bony posterior fossa area was also statistically smaller in fetuses with MMC but without Chiari II compared with controls, although the growth rate paralleled the control cases.

In contrast, and as predicted, cerebellar growth (as indicated by area of the vermis) showed no statistically significant differences between the control and the 2 MMC groups over the gestational ages studied.

It is also interesting to note that there was little or no correlation between the severity of the spinal malformation judged by the area of the neck of the sac, sac volume, and the size of the bony posterior fossa. The segmental level of the open spinal defect may have some influence on the development of Chiari II deformity. The majority of fetuses without a Chiari II deformity had an estimated open spinal defect at or below the level of the lumbosacral junction, although this was not an exclusive association.

In controls, the bony posterior fossa was significantly larger than the cerebellum at all gestational ages studied. In cases of MMC, the cerebellum is normal in size, but the posterior fossa is small. One explanation of this is that the normal bony posterior fossa growth depends primarily on pressure from CSF rather than expansion of the underlying cerebellum. Alternatively, secondary bony posterior fossa growth induction may depend on a chemical present in CSF that is not able to reach significant concentration because of the continuous CSF loss. This, however, is the only observation that led to McLone and Knepper suggesting the hydrostatic theory<sup>1</sup> and does not in itself imply any causal link between the MMC and the posterior fossa/hindbrain abnormalities. McLone and Knepper propose that failure to occlude the primitive central canal transiently during the first trimester because of the neural tube defect results in excessive drainage of CSF out of the spinal and cranial compartments. This, in turn, results in failure of distension of the rhombencephalic vesicle, which is necessary for normal induction of the posterior fossa mesenchyme, resulting in a small bony posterior fossa. An implication of this theory is that the 2 should be found together consistently, and in utero 23% of the fetuses studied did not have a Chiari II deformity, but the bony posterior fossa was reduced in size. The severity of the spinal abnormality did not correlate with the degree of size reduction of the posterior fossa, but transient closure of the primitive central canal may not depend on the severity of the spinal defect. A low-lying lumbosacral open spinal defect may provide some protection. McLone and Knepper's theory specifically relates to failed closure of the primitive central canal, but other factors such as the rate of continuous CSF loss through the open spinal defect following transient closure of the primitive central canal may also be important in Chiari II deformity development. Our study does not address rates of CSF loss across the spinal defect or CSF pressures within the subarachnoid space. Our findings raise some interesting questions about the causal relationship between open spinal dysraphism and Chiari II deformity and the current theoretical explanations.

## CONCLUSION

Not all fetuses (23%) with antenatally diagnosed open spinal dysraphism have a Chiari II deformity. Open spinal dysraphic processes produce a small posterior fossa, which is most severe in cases with hindbrain herniation. The bony posterior fossa is also significantly reduced in volume in cases of open spinal dysraphism without hindbrain herniation. This interesting observation adds to the discussion of the causality of Chiari II deformity. There does not appear to be simple linear correlation between the severity of the spinal malformation and the degree of bony posterior fossa restriction.

## Disclosures

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## COMMENT

This study summarizes the 10-year experience of antenatal ultrasonography on fetuses referred with lumbosacral spinal malformations confirmed as open spinal dysraphism. Sixty-five (65) fetuses with open

lumbosacral dysraphism who were imaged between 18 and 36 weeks gestation were compared with fetuses with normal brains and spines, which served as age-matched controls. The following data were recorded: the size of the spina bifida defect, maximum transverse diameter to the trigonal of the lateral ventricles, maximum depth of the subarachnoid space of the lateral surfaces at the cerebellar hemispheres, area of the cerebella vermis, area of the bony posterior fossa, as well as the absence or presence of a hindbrain malformation, as defined by any part of the cerebellum line, below a line joining the opisthion and basion. Statistical analyses were performed.

In this study, the size or volume of the spinal defect was found not to be a determining cause as to the presence or absence of the Chiari II deformity. In fetuses with Chiari II deformities, the trigones were statistically larger in the third trimester compared with the second trimester; however, there was no significant difference in the trigonal size in the third trimester in the myelomeningocele group without Chiari II deformities. Finally, the area of the bony posterior fossa was significantly reduced in all fetuses with myelomeningocele compared with the control groups. When stratified, with

myelomeningocele but no Chiari II deformity group were smaller than the control groups, but larger than the myelomeningocele with Chiari II deformity. Cerebellar growth rate was similar in all 3 groups.

As is exhibited by this study, intrauterine MRI is proving to be a valuable diagnostic tool for evaluating brain and spine pathology in the developing fetus with good accuracy. These data provide healthcare practitioners with valuable data by which to discuss the fetus' prognosis with the parent, and enable a more informed decision to be made regarding appropriate clinical decisions and planning to take place. Despite some limitations of the study, it remains important to use new technology to test the robustness of long-held theories. This study raises the question as to whether McLone's unified theory is more complicated than initially thought.

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