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# Prenatal brain imaging for predicting need for postnatal hydrocephalus treatment in fetuses that had neural tube defect repair *in utero*

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**KEYWORDS:** brain; fetal surgery; hydrocephalus; magnetic resonance imaging; myelomeningocele; neural tube defects; spina bifida; ventriculoperitoneal shunt

## ABSTRACT

***Objective*** *To determine if brain imaging in fetuses that underwent prenatal repair of neural tube defect (NTD) can predict the need for postnatal hydrocephalus treatment (HT) in the first year postpartum.*

***Methods*** *This was a retrospective study of fetuses diagnosed with open NTD that had* in-utero *myelomeningocele repair between April 2014 and April 2016. Independent variables were collected from four chronological sets of fetal images: presurgery ultrasound, presurgery magnetic resonance imaging (MRI), 6-week postsurgery MRI and predelivery ultrasound. The following independent variables were collected from all image sets unless otherwise noted: gestational age, head circumference, mean ventricular width, ventricular volume (MRI only), hindbrain herniation (HBH) score (MRI only), and level of lesion (LOL), defined as the upper bony spinal defect (presurgery ultrasound only). Based on these measurements, additional variables were defined and calculated including change in degree of HBH, ventricular width growth (mm/week) and ventricular volume growth (mL/week). The need for HT (by either ventriculoperitoneal shunt or endoscopic third ventriculostomy with choroid plexus cauterization) was determined by a pediatric neurosurgeon using clinical and radiographic criteria; a secondary analysis was performed using the MOMS trial criteria for hydrocephalus. The predictive value of each parameter was assessed by receiver–operating characteristics curve and logistic regression analyses.*

***Results*** *Fifty affected fetuses were included in the study, of which 32 underwent open hysterotomy and 18 fetoscopic repair. Two neonates from the open hysterotomy group died and were excluded from the analysis. The mean gestational ages for the presurgery ultrasound, presurgery MRI, postsurgery MRI and predelivery ultrasound were 21.8 ± 2.1, 22.0 ± 1.8, 30.4 ± 1.6 and 31.0 ± 4.9 weeks, respectively. A total of 16 subjects required HT. The area under the curve (AUC) of predictive accuracy for HT showed that HBH grading on postsurgery MRI had the strongest predictive value (0.86;* $P < 0.01$*), outperforming other predictors such as postsurgery MRI ventricular volume (0.73;* $P = 0.03$*), MRI ventricular volume growth (0.79;* $P = 0.01$*), change in HBH (0.82;* $P = 0.01$*), and mean ventricular width on predelivery ultrasound (0.73;* $P = 0.01$*). Other variables, such as LOL, mean ventricular width on presurgery ultrasound, mean ventricular width on presurgery and postsurgery MRI, and ventricular growth assessment by MRI or ultrasound, had AUCs < 0.7. Optimal cut-offs of the variables with the highest AUC were evaluated to improve prediction. A combination of ventricular volume growth ≥ 2.02 mL/week and/or HBH of 3 on postsurgery MRI were the optimal cut-offs for the best prediction (odds ratio (OR), 42 (95% CI, 4–431); accuracy, 84%). Logistic regression analyses showed that persistence of severe HBH 6 weeks after surgery by MRI is one of the best predictors for HT (OR, 39 (95% CI, 4–369); accuracy, 84%). There was no significant change in the results when the MOMS trial criteria for hydrocephalus were used as the dependent variable.*

***Conclusions*** *Persistence of HBH on MRI 6 weeks after prenatal NTD repair independently predicted the need*

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*for postnatal HT better than any ultrasound- or other MRI-derived measurements of ventricular characteristics. These results should aid in prenatal counseling and add support to the hypothesis that HBH is a significant driver of hydrocephalus in myelomeningocele patients.* 

## INTRODUCTION

Neural tube defects (NTD) affect approximately 1 in 2000 liveborn children[1]. Open defects, i.e. myelomeningocele (MMC), are associated with motor and cognitive deficits throughout development[2]. It is hypothesized that leakage of cerebrospinal fluid (CSF) can cause intracranial hypotension and result in a Chiari malformation Type II[3,4]. The hindbrain herniation (HBH) seen in this malformation[5] is caused by a downward displacement of the cerebellum below the level of the foramen magnum, and may result in a compressed brainstem, small posterior fossa and obstructed fourth ventricle[6]. This obstruction may prevent the movement of CSF and result in hydrocephalus[4,7].

A common treatment for hydrocephalus is the placement of a ventriculoperitoneal (VP) shunt. This intervention requires lifelong monitoring, and 75% of cases require a shunt revision[8,9]. In the MOMS trial, 82% of babies that underwent postnatal repair, *vs* 40% of those repaired prenatally, required VP shunting during the first year postpartum[10]. Moreover, significant hydrocephalus is associated with brainstem compression, a leading cause of death in infants with NTD[11,12].

Identifying infants with the greatest need for hydrocephalus treatment (HT) after prenatal MMC repair would help establish realistic expectations of the need for ongoing postnatal care and improve understanding of the underlying mechanisms involved. Different factors associated with higher risk for HT have been suggested, including more cephalad lesions that predict greater morbidity[13,14] and larger fetal ventricular size associated with higher risk for postnatal VP shunting[9,15]. Complicating this issue is that, in most studies, ventricular size is determined by a simple measurement of the ventricle at the atrial level using ultrasound or magnetic resonance imaging (MRI).

Combining multiple selected measurements from both ultrasound and MRI, before and after fetal NTD repair, in order to improve the ability to predict the need for postnatal HT, has not been reported previously. In this study, we sought to identify the best predictors of need for HT in babies with prenatal NTD repair, using imaging parameters obtained at different timepoints during pregnancy. We hypothesized that advanced prenatal imaging would provide an accurate method for identifying those fetuses with prenatally repaired NTD that are most likely to require postnatal HT and provide insight into the pathophysiology of hydrocephalus in the MMC population.

## METHODS

### Study population

This was a retrospective cohort study of 50 fetuses that underwent either fetoscopic or open hysterotomy MMC repair between April 2014 and April 2016. All fetuses that underwent a prenatal NTD repair met the MOMS trial inclusion criteria[10] (singleton pregnancy, MMC with the upper boundary located between T1 and S1, evidence of HBH, gestational age between 19.0 and 25.9 weeks, normal karyotype, maternal age $\geq$ 18 years) and none of the exclusion criteria (fetal anomalies unrelated to spina bifida, severe kyphosis, risk of preterm birth including short cervix and previous preterm birth, placental abruption, body mass index $\geq 35\,kg/m^2$ and contraindication to surgery, including previous hysterotomy in the active uterine segment). All patients agreed to open fetal surgery before they were offered the experimental fetoscopic procedure. Patients underwent preoperative fetal echocardiography, comprehensive ultrasound scan and MRI. They were managed per our standard protocol involving steroid administration, prophylactic tocolytic agents and antibiotics[16]. Fetoscopic repair was performed under a Federal Drug Administration Investigational Drug Exemption (no. G140201). All women provided written informed consent to participate in this study, which was approved by the Baylor College of Medicine Institutional Review Board (IRB H-34680). Fetal cases of open NTD were diagnosed at the Texas Children's Fetal Center – Texas Children's Hospital Pavilion for Women.

Fetoscopic repair was performed via a laparotomy with an exteriorized uterus as reported elsewhere[16]. Partial uterine $CO_2$ insufflation was carried out using a heater–humidifier (Insuflow, Lexion Medical, St Paul, MN, USA). Open repair was performed by an open hysterotomy approach using similar methodology to that used in the MOMS trial[10]. Data for these patients were acquired retrospectively under a separate IRB-approved protocol (H-38479).

### Diagnosis and presurgery image acquisition

Detailed presurgical transabdominal ultrasound examination (presurgery ultrasound) was performed in all pregnancies referred with the diagnosis of NTD in order to establish eligibility for prenatal MMC repair (Voluson E8, GE Healthcare Ultrasound, Milwaukee, WI, USA). Assessment was performed of fetal biometry, brain anatomy, level of the lesion (LOL) defined as the upper bony spinal defect, and any potentially associated malformations. Fetal biometry data were compared with the INTERGROWTH-21$^{st}$ (IG21) standards[17].

Immediately after the presurgery ultrasound ($\pm$ 2 days), patients underwent fetal MRI (presurgery MRI) using a 1.5-T Phillips Ingenia scanner, software version 5.1.7 (Phillips North America, Andover, MA, USA). All MRI studies were performed without maternal or

 

fetal sedation. A combined six-channel body array coil was positioned over the lower pelvic area of the patient for optimal signal. After imaging localization, non-breath-hold T2-weighted single-shot fast spin echo sequences of the entire fetus were obtained in three orthogonal planes (axial, coronal, sagittal). All diagnostic sequences were performed using 4-mm slice thickness, 1.5-mm slice overlap, 1050 ms repetition time and 140 ms echo time. Acquisition time was approximately 45 s per orthogonal plane. Additional images acquired included isotropic volumetric T1-weighted sequence echo planar imaging and diffusion-weighted imaging of the fetal brain for the evaluation of blood products and ischemia, respectively. MRI used the following settings in all cases: field of view, 280 mm × 280 mm; matrix, 128 × 128; voxel size, 2.5 mm × 2.5 mm × 4.0 mm. Total acquisition time was limited to 60 min.

### Postsurgery image acquisition

Six weeks following surgery, a second fetal MRI (postsurgery MRI) was performed using the same equipment and settings as for the presurgery MRI. This is part of our clinical follow-up protocol for all patients who undergo a prenatal MMC repair.

Information was also obtained from the transabdominal ultrasound scan most proximate to delivery (predelivery ultrasound) using the same equipment and settings as in the presurgery ultrasound scan. Fetal biometrics were also obtained and compared with IG21 standards[17].

### Ventricular width

The width of the lateral ventricle posterior horns imaged on presurgery ultrasound, presurgery MRI, postsurgery MRI and predelivery ultrasound were measured bilaterally, using a previously established method[18] (Figures 1 and S1). The average measurement of the two sides was used in the analysis.

### Hindbrain evaluation

Evaluation of the fetal MRI for posterior fossa and craniocervical-junction landmarks was performed by an experienced pediatric neuroradiologist blinded to patient outcomes and type of surgery. The pre- and postsurgical MRI images were evaluated for any anatomical markers of Chiari II malformation, presence and degree of HBH, as well as degree of reversal of HBH after surgical repair (Figure S1). The standard postsurgery MRI evaluation included, first, the identification of persistent HBH as defined by the cerebellar tonsils being seen below the level of the foramen magnum, and second, reversal of HBH, as defined by the cerebellar tonsils being seen above the level of the foramen magnum. A modified version of the grading system of Sutton *et al.*[19] was used for this evaluation. Modifications included the incorporation of normal and minor findings (such as tectal beaking and vertical tectum) into Grade 0, and codifying the degree of HBH severity (using the level above or below C1 posterior arch). Our modified grading system was as follows: Grade 0: normal posterior fossa or tectal beaking without HBH or extra-axial space effacement; Grade 1: effacement of the fourth ventricle and/or cisterna magna without HBH; Grade 2: HBH above the C1 posterior arch but below the foramen magnum; and Grade 3: HBH below C1 posterior arch (Figure 2).

### Fetal brain ventricular volumetry

Volumetric assessment of the fetal brain ventricular system was performed using T2-weighted images from the pre- and postsurgery MRIs. Ventricular volumetry was performed using previously reported methods[20] (Figure S1). Super-resolution reconstruction was performed according to previously published protocols[21]. Processed images were analyzed using postprocessing manual segmentation with Amira 6.0 software (FEI Visualization Sciences Group, Hillsboro, OR, USA). Ventricular volume was calculated based on manual delineation

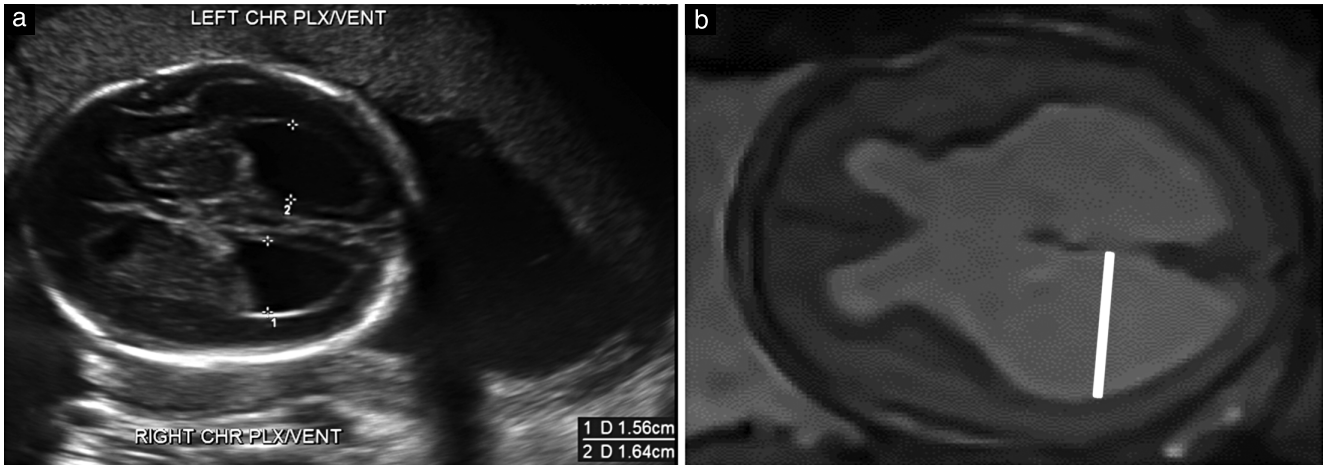


**Figure 1** Ventricular width measurement by ultrasound (a) and magnetic resonance imaging (MRI) (b). (a) Prenatal ultrasound scan showing axial transventricular view of fetal brain at 26.2 weeks' gestation; calipers indicate measurement of ventricular widths. (b) Fetal T2-weighted MRI performed at 24.1 weeks' gestation showing bilateral ventriculomegaly; line demonstrates measurement of ventricular width.

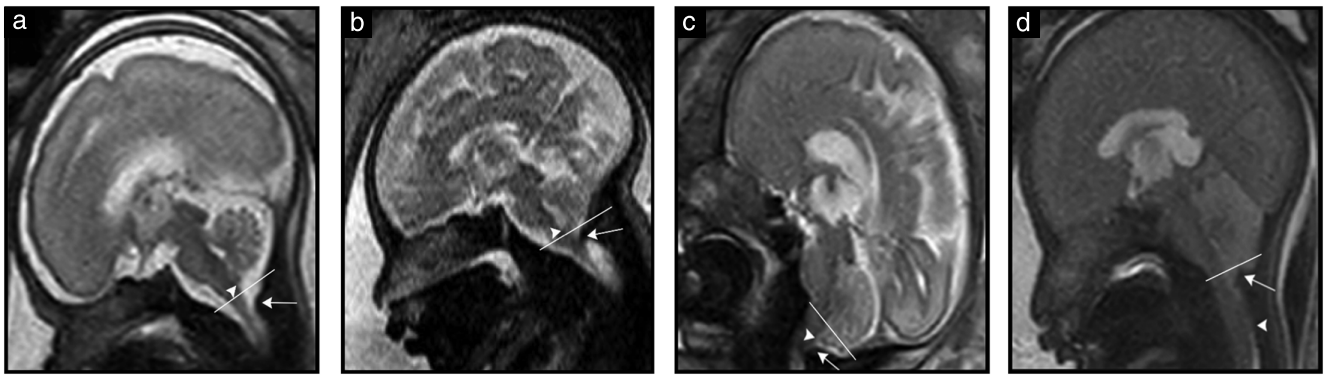


**Figure 2** Fetal magnetic resonance images in sagittal midline view demonstrating modified hindbrain herniation (HBH) scoring system followed in this study. Level of foramen magnum (line), C1 posterior arch (arrow) and lower tip of cerebellar tonsils (arrowhead) were identified in all images. (a) Grade 0: no HBH and no extra-axial space effacement. (b) Grade 1: effacement of cisterna magna and/or fourth ventricle without HBH. (c) Grade 2: HBH below foramen magnum but above C1 posterior arch. (d) Grade 3: HBH below C1 posterior arch.

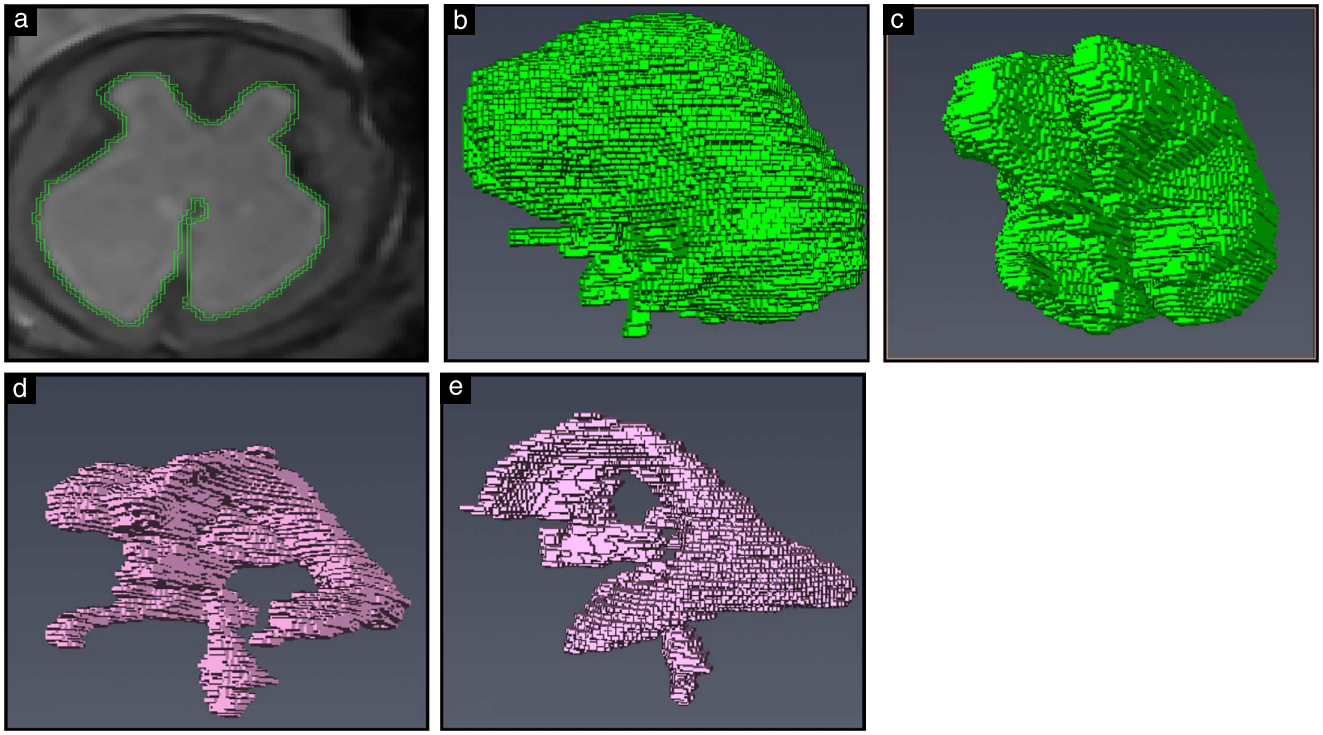


**Figure 3** (a–c) Presurgery fetal magnetic resonance imaging performed at 24.1 weeks' gestation in fetus with neural tube defect: (a) delineation of ventricular system to assess ventricular volume; (b,c) 3D volumetric reconstruction from manual delineation of ventricular system showing severe ventriculomegaly. (d,e) 3D volumetric reconstruction from manual delineation of normal ventricular system volume. All delineations and 3D volume reconstructions were created using Amira 6.0 software.

of the ventricular system (Figure 3) using the Material Statistics tool in Amira.

Examiners performing the MRI and ultrasound image analysis were blinded to patient outcome and the type of surgery performed.

### Comparison between pre- and postsurgery measurements

The following formula was used for comparison between the two imaging measurements:

Change in the degree of HBH = postsurgery MRI HBH score – presurgery MRI HBH score.

In order to assess any change over time (growth), differences in successive measurements were divided by the time interval (in weeks):

(1) Ventricular volume growth = (postsurgery MRI ventricular volume – presurgery MRI ventricular volume)/duration (weeks) between the two MRI scans.

(2) Ventricular growth by MRI = (postsurgery MRI mean ventricular width – presurgery MRI mean ventricular width)/duration (weeks) between the two MRI scans.

(3) Ventricular growth by ultrasound = (predelivery ultrasound mean ventricular width – presurgery ultrasound mean ventricular width)/duration (weeks) between the two ultrasound scans.

A complete list of all independent variables collected from the pre- and postsurgery ultrasound and MRI scans is provided in Appendix S1.

### Perinatal results and neurosurgery assessment

Patients were followed up in our institution in the multidisciplinary Spina Bifida Clinic or by the pediatric neurosurgeon at the referring center. The decision regarding need for HT was made by our neurosurgeon or, in most cases, by the neurosurgeon of the referring center in consultation with our neurosurgeon. Need for HT was determined using standard clinical and radiographic criteria, and either a VP shunt or an endoscopic third ventriculostomy with choroid plexus cauterization was performed. Endoscopic third ventriculostomy encompasses an ostomy through the floor of the third ventricle into the prepontine cistern allowing CSF to bypass the obstruction to its normal pathway[22,23]. Choroid plexus cauterization reduces the amount of CSF produced by the choroid plexus[23]. A secondary analysis of need for VP shunt placement was performed using the MOMS trial criteria for hydrocephalus[10] (Appendix S2).

### Statistical analysis

Data analysis was performed using SPSS Statistics version 21.0 (IBM Corp., Armonk, NY, USA). Quantitative variables were expressed as mean ± SD if they had a normal distribution (by Kolmogorov–Smirnov test) and as median (range) if they had a non-normal distribution. Student's *t*-test for independent samples and Pearson's $\chi^2$ or Fisher's exact test were used to compare quantitative and qualitative data, respectively. The Wilcoxon rank-sum test was used for comparison between quantitative variables that did not have a normal distribution. The predictive value of each parameter (presurgery and predelivery ultrasound ventricular widths, LOL by presurgery ultrasound, presurgery and postsurgery MRI ventricular widths, ventricular growth by ultrasound and by MRI, degree of HBH and change in degree of HBH, ventricular volume and ventricular volume growth) was assessed by receiver–operating characteristics curve analysis. Binary logistic regression models were used to compute the predictive values expressed as the odds ratio (OR) and 95% CI for individual and combined test variables. Sensitivity, specificity, positive predictive value (PPV), negative predictive value and accuracy values were calculated using MedCalc software (MedCalc Software, Ostend, Belgium). Results were considered to be significant at a *P*-value $< 0.05$.

## RESULTS

A total of 50 women were included in the study, of whom 18 underwent fetoscopic and 32 open hysterotomy fetal MMC repair. Mean gestational ages at presurgery ultrasound, presurgery MRI, postsurgery MRI and predelivery ultrasound were 21.8 ± 2.1, 22.0 ± 1.8, 30.4 ± 1.6 and 31.0 ± 4.9 weeks, respectively. Neonatal

**Table 1** Presurgery ultrasound and magnetic resonance imaging (MRI) data of 48 fetuses that underwent prenatal myelomeningocele repair, according to whether they required hydrocephalus treatment (HT) during the first year postpartum

| *Characteristic* | *No hydrocephalus treatment* (n = *32*) | *Hydrocephalus treatment* (n = *16*) | P* |
|---|---|---|---|
| Presurgery ultrasound | | | |
| GA at ultrasound (weeks) | 21.7 ± 2.1 | 22.5 ± 1.8 | 0.2 |
| Head circumference (mm) | 178.9 ± 20.3 | 194.6 ± 21.4 | 0.02 |
| Head-circumference percentile† | 15.0 (0.01–84.74) | 25.1 (0.16–65.2) | 0.03 |
| Mean ventricular width (mm) | 9.8 ± 3.1 | 11.9 ± 3.6 | 0.04 |
| Mean ventricular width | | | |
| ≥ 10 mm | 15/32 (47) | 11/16 (69) | 0.2 |
| ≥ 15 mm | 1/32 (3) | 4/16 (25) | 0.04 |
| Level of lesion L3 or lower‡ | 30/32 (94) | 9/16 (56) | < 0.01 |
| Presurgery MRI | | | |
| GA at MRI (weeks) | 21.9 ± 1.8 | 22.7 ± 1.5 | 0.1 |
| Head circumference (mm) | 177 ± 18 | 193 ± 18 | 0.08 |
| Mean ventricular width (mm) | 10.1 ± 2.7 | 11.9 ± 4.0 | 0.1 |
| Mean ventricular width | | | |
| ≥ 10 mm | 15/32 (47) | 10/16 (63) | 0.4 |
| ≥ 15 mm | 0/32 (0) | 4/16 (25) | < 0.01 |
| Ventricular volume (mL) | 12.1 ± 7 | 17.7 ± 11.5 | 0.1 |
| Hindbrain herniation score§ | 3 (1–3) | 3 (2–3) | 0.3 |
| Hindbrain herniation¶ | 32/32 (100) | 16/16 (100) | — |

Data are presented as mean ± SD, median (range) or *n*/*N* (%). *Subjects that did not require HT *vs* those that received HT in first year postpartum; Student's *t*-test for independent samples or Wilcoxon rank sum test and Pearson's $\chi^2$ or Fisher's exact test used to compare quantitative and qualitative data, respectively. †Percentiles based on INTERGROWTH-21st standards[17]. ‡Level of lesion range: no HT, L2–S1; HT, T9–L4. §Determined by pediatric neuroradiologist using adaptation of Sutton *et al.*[19] hindbrain herniation (HBH) scoring system; HBH score defined as: 0, normal posterior fossa or tectal beaking without HBH or extra-axial space effacement; 1, effacement of the fourth ventricle and/or cisterna magna without HBH; 2, HBH above C1 posterior arch; and 3, HBH below C1 posterior arch. ¶Cases with confirmed hindbrain herniation diagnosis on assessment by pediatric neuroradiologist. GA, gestational age.

death occurred in two babies from the open hysterotomy group that were born at 24.3 and 27.3 weeks' gestation, respectively; these cases were excluded from the prediction analysis. The 48 remaining patients were split into two groups, those who received HT during the first year postpartum ($n = 16$) and those who did not ($n = 32$). No significant differences were found between the two groups in maternal demographic parameters (Table S1) or in the type of NTD repair technique (fetoscopic *vs* open) performed (Table S2).

Fetal baseline characteristics at diagnosis, as provided by the presurgery ultrasound and MRI examinations, are presented in Table 1. The proportion of fetuses with a lesion at or lower than L3 was significantly higher in the non-HT group (94%) as compared with the HT group (56%; $P < 0.01$). Gestational age at presurgery ultrasound and MRI assessments was comparable between the two groups. Head circumference and mean ventricular width measured at the presurgery ultrasound scan were significantly higher in the HT group than in the non-HT group. The HT group had a significantly higher proportion of cases with signs of severe ventriculomegaly (ventricular width $\geq 15$ mm) evidenced by both presurgery ultrasound and MRI. All other measurements, including initial assessment of HBH and ventricular volume, were comparable between the two groups.

The results from the postsurgery MRI and predelivery ultrasound are presented in Table 2. Four subjects that underwent presurgery MRI did not have a postsurgery MRI scan as they were born prior to 6 weeks postoperatively. The gestational ages at the predelivery ultrasound and postsurgery MRI assessments were comparable between the two groups. The HBH score was significantly higher (suggestive of persistent HBH) at postsurgery MRI in those patients that ultimately required HT. This group also had a less pronounced change between the presurgery and postsurgery HBH assessments as compared with fetuses that did not require HT (Table 2). Furthermore, ventricular volume and ventricular volume growth (as assessed by MRI) were significantly greater in the group that needed HT. Similar findings were observed on predelivery ultrasound, with the mean ventricular width and the change in ventricular width before and after surgery being significantly higher in fetuses that required HT compared with those that did not.

All 16 (100%) neonates in the HT group met the MOMS criteria of need for HT, while only six (19%) met the same criteria in the non-HT group ($P < 0.01$) (Table 3). Details of the neurosurgery assessment and perinatal outcomes of the two groups are provided in Tables 3 and S2, respectively.

### Prediction of need for hydrocephalus treatment

Of all the parameters evaluated in this study, the best predictors of need for HT are presented in Table 4, based on area under the curve (AUC) analyses. The two best individual predictors of the need for HT were, first, the degree of HBH (represented by the postsurgery HBH score and the change in HBH score before and after surgery), and second, the change in ventricular volume on MRI before and after surgery. Postsurgery MRI HBH score had the strongest individual predictive value (0.86; $P < 0.01$), outperforming other predictors such as postsurgery MRI ventricular volume (0.73; $P = 0.03$), ventricular volume growth (0.79; $P = 0.01$), change in HBH score from presurgery to postsurgery MRI (0.82; $P = 0.01$) and mean ventricular width on predelivery ultrasound (0.73; $P = 0.01$). All other variables evaluated, including LOL, predelivery ultrasound mean ventricular width and ventricular growth by MRI or ultrasound, had an AUC $< 0.7$. Optimal cut-offs of the variables with the highest AUCs were evaluated to improve prediction (Figure 4). Ventricular volume growth rate of $\geq 2.02$ mL/week and/or postsurgery HBH below C1 posterior arch (Grade 3) were the optimal cut-offs to achieve the best prediction model.

When the predictive value of previously published clinical cut-offs proposed as markers for increased risk of need for HT were compared with the cut-offs obtained from this analysis (Table 5), the three most accurate predictors were (1) the combination of change in ventricular volume $\geq 2.02$ mL/week and/or postsurgery HBH score of 3 (OR, 42; accuracy, 84%); (2) the detection of cerebellar tonsils below C1 level (HBH Grade 3) after surgery (OR, 39; accuracy, 84%); and (3) the lack of HBH reversal assessment (OR, 28; accuracy, 85%). These parameters had a stronger predictive value for need for HT than did the commonly used parameters such as mean ventricular width $\geq 15$ mm before surgery (on ultrasound: OR, 10; accuracy, 73%), after surgery (on MRI: OR, 1.5; accuracy, 57%) or proximate to delivery (on ultrasound: OR, 3; accuracy, 63%). The highest PPVs were obtained from a HBH score of 3 after surgery (89%), a lack of HBH reversal per standard clinical assessment (80%) and a presurgery ultrasound evaluation mean ventricular width $\geq 15$ mm (80%).

Similar results were found when the same analysis was performed using MOMS trial criteria for need for HT. The best predictive values were observed for the combination of change in ventricular volume $\geq 2.02$ mL/week and/or postsurgery HBH score of 3 (OR, 28 (95% CI, 4–196.5); accuracy, 84%), followed by MRI-derived HBH score of 3 at 6 weeks postsurgery (OR, 17 (95% CI, 1.9–157.2); accuracy, 72%), and the persistence of HBH after surgery by clinical assessment (OR, 17 (95% CI, 3.1–88.8); accuracy, 77%) (Table S3).

## DISCUSSION

Our findings indicate that the best predictors of subsequent need for HT in babies undergoing fetal MMC repair are significant growth ($> 2.02$ mL/week) in ventricular volume, 6-week postsurgery MRI showing persistence of HBH below the level of the C1 posterior arch and lack of reversal of HBH, and mean ventricular width $\geq 15$ mm on presurgery ultrasound.

**Table 2** Postsurgery magnetic resonance imaging (MRI) and predelivery ultrasound (US) data of 48 fetuses that underwent prenatal myelomeningocele repair, according to whether they required hydrocephalus treatment (HT) during first year postpartum

| *Characteristic* | *No hydrocephalus treatment* | *Hydrocephalus treatment* | P* |
|---|---|---|---|
| Postsurgery MRI | | | |
| *n*† | 30 | 14 | |
| GA at MRI (weeks) | 30.6 ± 1.7 | 30 ± 1.6 | 0.3 |
| Head circumference (mm) | 284.1 (243 to 307.7) | 283.0 (252.6 to 323.1) | 0.9 |
| Mean ventricular width (mm) | 13.3 (7.8 to 25.9) | 14.4 (10.2 to 33.1) | 0.1 |
| Mean ventricular width | | | |
| ≥ 10 mm | 26/30 (87) | 14/14 (100) | 0.3 |
| ≥ 15 mm | 12/30 (40) | 7/14 (50) | 0.7 |
| Ventricular volume (mL) | 22 (13 to 72.3) | 33.6 (14.1 to 197.8) | 0.03 |
| Hindbrain herniation score‡ | 0 (0 to 3) | 3 (0–3) | < 0.01 |
| Hindbrain herniation§ | 8/30 (27) | 12/14 (86) | < 0.01 |
| Ventricular volume growth (mL/week) | 1.2 (0.7 to 6) | 2.3 (0.9 to 21.4) | 0.01 |
| Ventricular width growth (mm/week) | 0.4 (−0.2 to 1.5) | 0.7 (0.1 to 2.3) | 0.08 |
| Change in hindbrain herniation score between presurgery and postsurgery MRI | −2 (−3 to 0) | 0 (−3 to 1) | < 0.01 |
| Predelivery US | | | |
| *n* | 32 | 16 | |
| GA at ultrasound (weeks) | 30.6 ± 5.0 | 32.6 ± 3.6 | 0.15 |
| Head circumference (mm) | 292.7 (164.9 to 342.2) | 298.8 (219.6 to 402.8) | 0.1 |
| Head-circumference percentile (mm)¶ | 55.6 (0.21 to 99.9) | 70.1 (2.81 to 100) | 0.2 |
| Mean ventricular width (mm) | 13.8 (7.9 to 22.4) | 19 (4.3 to 43.8) | < 0.01 |
| Mean ventricular width | | | |
| ≥ 10 mm | 25/32 (78) | 15/16 (94) | 0.2 |
| ≥ 15 mm | 13/32 (41) | 11/16 (69) | 0.1 |
| Ventricular width growth (mm/week) | 0.54 ± 0.4 | 0.88 ± 0.7 | 0.04 |

Data are presented as mean ± SD, median (range) or *n*/*N* (%). *Subjects that did not require HT *vs* those that received HT in first year postpartum; Student's *t*-test for independent samples or Wilcoxon rank sum test and Pearson's $\chi^2$ or Fisher's exact test used to compare quantitative and qualitative data, respectively. †Four subjects that underwent presurgery MRI did not have postsurgery MRI as they were born prematurely before that timepoint. ‡Determined by pediatric neuroradiologist using adaptation of Sutton *et al.*[19] hindbrain herniation (HBH) scoring system; HBH score defined as: 0, normal posterior fossa or tectal beaking without HBH or extra-axial spaces effacement; 1, effacement of the fourth ventricle and/or cisterna magna without HBH; 2, HBH above C1 posterior arch; and 3, HBH below C1 posterior arch. §Cases with confirmed hindbrain herniation diagnosis on assessment by pediatric neuroradiologist. ¶Percentiles based on INTERGROWTH-21st standards[17]. GA, gestational age.

**Table 3** Neurosurgery assessment and postnatal intervention in 48 infants that underwent prenatal myelomeningocele repair, according to whether they required hydrocephalus treatment (HT) during first year postpartum

| *Variable* | *No hydrocephalus treatment (n = 32)* | *Hydrocephalus treatment (n = 16)* | P* |
|---|---|---|---|
| Met MOMS criteria for hydrocephalus† | 6/32 (19) | 16/16 (100) | < 0.01 |
| Type of therapy | | | |
| ETV/CPC | — | 10/16 (63) | — |
| VP shunt | — | 6/16 (37) | — |
| Average age at therapy (days) | | | |
| ETV/CPC | — | 101.1 ± 98.1 | — |
| VP shunt | — | 75.8 ± 52 | — |
| Repair of dehiscence | 1/32 (3) | 8/16 (50) | < 0.01 |
| Type of dehiscence repair | | | |
| Bedside repair | 1/32 (3) | 6/16 (37) | < 0.01 |
| Repair in operating room | 0/32 (0) | 2/16 (13) | 0.11 |
| CSF leakage at birth | 1/32 (3) | 8/16 (50) | < 0.01 |

Data presented as *n*/*N* (%) or mean ± SD. *Subjects that did not require HT *vs* those that received HT in first year postpartum; Pearson's $\chi^2$ or Fisher's exact test used to compare qualitative data. †As defined by Management of Myelomeningocele Study (MOMS) trial[10]. CSF, cerebrospinal fluid; ETV/CPC, endoscopic third ventriculostomy/choroid plexus cauterization; VP, ventriculoperitoneal.

**Table 4** Predictive value of common diagnostic imaging parameters for need for hydrocephalus treatment within first year postpartum in fetuses that underwent prenatal myelomeningocele repair

| *Predictor* | *AUC (95% CI)* | P | *Odds ratio (95% CI)* | P |
|---|---|---|---|---|
| HBH score on postsurgery MRI and MRI ventricular volume growth* | 0.91 (0.80–1.00) | < 0.01 | 26.12 (7.61–98.91) | < 0.01 |
| HBH score on postsurgery MRI | 0.86 (0.73–0.99) | < 0.01 | 4.15 (1.94–8.86) | < 0.01 |
| Change in HBH score on MRI | 0.82 (0.67–0.97) | 0.01 | 3.42 (1.71–6.82) | < 0.01 |
| Ventricular volume growth on MRI (mL/week) | 0.79 (0.62–0.97) | 0.01 | 1.49 (0.93–2.42) | < 0.01 |
| Mean ventricular width on predelivery US | 0.73 (0.57–0.89) | 0.01 | 1.17 (1.03–1.32) | 0.01 |
| Ventricular volume (mL) on postsurgery MRI | 0.73 (0.55–0.91) | 0.03 | 1.03 (0.99–1.07) | 0.09 |
| Level of lesion L3 or lower on presurgery US | 0.69 (0.51–0.86) | 0.04 | 11.67 (2.05–66.41) | < 0.01 |
| Ventricular growth on MRI | 0.67 (0.48–0.85) | 0.08 | 3.61 (0.84–15.35) | 0.08 |
| Ventricular volume (mL) on presurgery MRI | 0.66 (0.46–0.86) | 0.13 | 1.08 (0.98–1.18) | 0.12 |
| Ventricular growth on US | 0.65 (0.47–0.82) | 0.10 | 3.62 (0.95–13.72) | 0.05 |
| Mean ventricular width on postsurgery MRI | 0.64 (0.47–0.81) | 0.14 | 1.11 (0.99–1.24) | 0.08 |
| Mean ventricular width on presurgery US | 0.67 (0.51–0.84) | 0.18 | 1.23 (1.01–1.49) | 0.04 |
| Mean ventricular width on presurgery MRI | 0.62 (0.43–0.82) | 0.18 | 1.19 (0.98–1.44) | 0.08 |

HBH score defined as: 0, normal posterior fossa or tectal beaking without HBH or extra-axial space effacement; 1, effacement of fourth ventricle and/or cisterna magna without HBH; 2, HBH above C1 posterior arch; and 3, HBH below C1 posterior arch. Areas under the curve (AUC) were obtained from receiver–operating characteristics curves and *P* represents their level of significance. Odds ratios were obtained by binary logistic regression, including having hydrocephalus treatment within first 12 months postpartum as dependent variable and each variable as covariate; *P* represents level of significance for that prediction. *Combination of two independent variables with highest AUC. HBH, hindbrain herniation; MRI, magnetic resonance imaging; US, ultrasound.

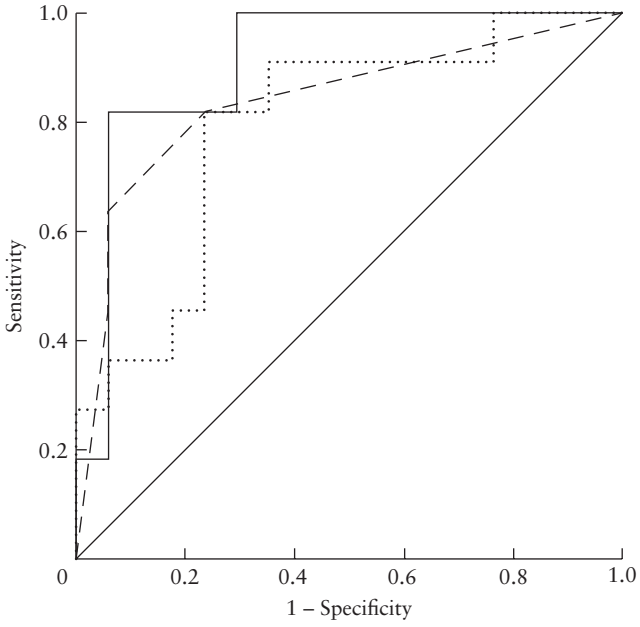


**Figure 4** Receiver–operating characteristics curves of variables with best predictive value for need for hydrocephalus treatment within 12 months after birth in fetuses that underwent prenatal myelomeningocele repair: hindbrain herniation score on post-surgery magnetic resonance imaging (MRI) (— —; area under the curve (AUC) = 0.86), ventricular volume growth on MRI (·····; AUC = 0.79), and their combination (——; AUC = 0.91).

We have shown that baseline characteristics prior to prenatal MMC repair, such as mild ventriculomegaly (width > 10 mm and < 15 mm), or the severity of the degree of HBH, have limited predictive value, in accordance with prior studies[9,13]. The best predictor of the need for HT at ≤ 12 months postpartum in the complete MOMS trial cohort was presurgery ventricular width, when multiple variables were included in the predictive model[9]. Our results corroborate these findings that presurgery ventricular width had the best predictive value of the parameters, and that the LOL and/or severity of presurgery HBH have very poor predictive accuracy. The only presurgery parameter that we identified as an acceptable predictor of need for HT was a mean ventricular width ≥ 15 mm on presurgery ultrasound making this the best predictor to use in settings with limited access to fetal MRI (PPV = 80%).

Our findings suggest that the best individual parameter for predicting the need for HT at ≤ 12 months is persistent HBH shown on MRI 6 weeks after surgery. Our modified scoring system is more applicable than previously described systems[19], because it takes into account the severity of the HBH in both pre- and postsurgical imaging assessments, includes unique scoring based on location of the cerebellar tonsils, and excludes other features not indicative of the severity of HBH. We confirmed our hypothesis that *a-priori* higher grades of HBH correlate with postnatal need for HT because of a more significant CSF obstruction and that cerebellar herniation above C1 is not, while herniation below C1 is, an independent predictor of HT.

The persistence of severe HBH (Grade 3) postoperatively had the highest PPV, with 89% requiring HT at ≤ 12 months. A similar PPV (80%) was seen when failure of HBH reversal was established by standard clinical criteria. Given the high predictive value of this marker, we suggest that management protocols for these patients include postoperative evaluation of HBH. Our results highlight the advantages of a second MRI assessment 6 weeks after fetal surgery to evaluate any changes in brain findings. Since prior studies have used information obtained from presurgery MRI only to predict the need for

 

**Table 5** Predictive value of categorical variables based on prenatal imaging (ultrasound (US) and magnetic resonance imaging (MRI)) for need for hydrocephalus treatment

| *Predictor* | *Odds ratio (95% CI)* | P* | *Sensitivity (95% CI) (%)* | *Specificity (95% CI) (%)* | *PPV (95% CI) (%)* | *NPV (95% CI) (%)* | *Accuracy (95% CI) (%)* |
|---|---|---|---|---|---|---|---|
| Ventricular volume growth ≥ 2.02 mL/week and/or post-surgery HBH score of 3 | 42.25 (4.14–430.88) | < 0.01 | 92.86 (66.13–99.82) | 76.47 (50.1–93.19) | 76.47 (57.67–88.57) | 92.86 (65.88–98.87) | 83.87 (66.27–94.55) |
| Postsurgery HBH score of 3 | 38.66 (4.07–369.46) | < 0.01 | 57.14 (28.86–82.34) | 96.67 (82.78–99.92) | 88.89 (52.49–98.30) | 84.09 (69.93–93.36) | 84.09 (69.93–93.36) |
| Non-reversal of HBH (clinical assessment) | 28.00 (5.42–144.72) | < 0.01 | 75.00 (47.62–92.73) | 90.32 (74.25–97.96) | 80.00 (56.81–92.4) | 87.5 (74.83–94.28) | 85.11 (71.69–93.8) |
| Ventricular volume growth ≥ 2.02 mL/week | 14.62 (2.19–97.61) | < 0.01 | 81.82 (48.22–97.72) | 76.47 (50.1–93.19) | 69.23 (47.75–84.71) | 86.67 (64.35–95.9) | 78.57 (59.05–91.7) |
| Mean ventricular width ≥ 15 mm on presurgery US | 10.33 (1.05–102.08) | 0.04 | 25.00 (7.27–52.38) | 96.88 (83.78–99.92) | 80.00 (32.71–97.05) | 72.09 (65.91–77.53) | 72.92 (58.15–84.72) |
| Mean ventricular width ≥ 10 mm on predelivery US | 4.2 (0.47–37.56) | 0.19 | 93.75 (69.77–99.84) | 21.88 (9.28–39.97) | 37.5 (32.44–42.85) | 87.5 (48.46–98.12) | 45.83 (31.37–60.83) |
| Mean ventricular width ≥ 15 mm on predelivery US | 3.21 (0.90–11.46) | 0.07 | 68.75 (41.34–88.98) | 59.38 (40.64–76.3) | 45.83 (33.17–59.06) | 79.17 (63.5–89.25) | 62.5 (47.35–76.05) |
| Mean ventricular width ≥ 10 mm on presurgery US | 2.49 (0.70–8.83) | 0.15 | 68.75 (41.34–88.98) | 53.12 (34.74–70.91) | 42.31 (30.89–54.61) | 77.27 (60.53–88.29) | 58.33 (43.21–72.39) |
| Presurgery HBH score of 3 | 2.27 (0.53–9.69) | 0.26 | 81.25 (54.35–95.95) | 34.38 (18.57–53.19) | 38.24 (30.50–46.61) | 78.57 (54.3–91.88) | 50.00 (35.23–64.77) |
| Presurgery HBH score of 2 | 0.51 (0.12–2.19) | 0.36 | 18.75 (4.05–45.65) | 68.75 (49.99–83.88) | 23.08 (8.74–48.46) | 62.86 (54.85–70.22) | 52.08 (37.19–66.71) |
| Mean ventricular width ≥ 10 mm on presurgery MRI | 1.88 (0.55–6.44) | 0.31 | 62.5 (35.43–84.8) | 53.12 (34.74–70.91) | 40.00 (28.2–53.09) | 73.91 (58.18–85.23) | 56.25 (41.18–70.52) |
| Mean ventricular width ≥ 15 mm on postsurgery MRI | 1.5 (0.42–5.38) | 0.53 | 50.00 (23.04–76.96) | 60.00 (40.6–77.34) | 36.84 (22.76–53.59) | 71.00 (58.53–82.41) | 56.82 (41.03–71.65) |

*Level of significance obtained from binary logistic regressions introducing hydrocephalus treatment as the dependent variable and each categorical variable as the covariate. Hindbrain herniation (HBH) score defined as: 0, normal posterior fossa or tectal beaking without HBH or extra-axial spaces effacement; 1, effacement of the fourth ventricle and/or cisterna magna without HBH; 2, HBH above C1 posterior arch; and 3, HBH below C1 posterior arch. Sensitivity: probability that test result will be positive when disease is present. Specificity: probability that test result will be negative when disease is not present. Positive predictive value (PPV): probability that disease is present when test is positive. Negative predictive value (NPV): possibility that disease is not present when test is negative. Accuracy: overall probability that patient will be classified correctly.

HT[9], comparability is limited. Based on McLone's Unified Theory[4], we speculate that the observed changes in HBH and/or the changes in ventricular volume reflect the effect of the prenatal repair on CSF hydrodynamics. There is a strong association between the degree of HBH, the degree of ventricular dilatation, and its progression[24]. MMC repair in the second trimester may prevent the leakage of spinal fluid, preventing the cerebellar herniation[19,25]. These changes are not seen in a postnatal repair. In the MOMS trial, 76% of the prenatally repaired cases had either no sign or only mild signs of HBH after birth, whereas the majority (96%) of postnatal repairs had persistent HBH[10]. Although, ventriculomegaly once established does not appear to resolve[19], the modification in postoperative CSF hydrodynamics may decrease the rate of ventricular dilatation and potentially improve the degree of cerebellar herniation. There is evidence suggesting a prolongation of the interval between birth and shunting in prenatally repaired cases when compared with those that do not have fetal repair[26]. The degree of change in HBH and ventricular volume after surgery may thus reflect normalization of CSF circulation and could be better surrogate markers of ventricular growth after birth than any preoperative parameter.

A secondary analysis was conducted using the definition of hydrocephalus of the MOMS trial, which provides objective indications for shunting. As a result of practice variation and increasing conservative approach to shunting, 25% of the prenatally repaired cases in the MOMS trial that fulfilled the criteria did not have a shunt placement[15]. Similarly, 25% of our cases met MOMS criteria but did not get treatment. Looking at fulfillment of the criteria for shunting, the same predictive factors applied as for those who actually received treatment.

Ventriculomegaly and HBH were the primary brain anomalies identified. Other structural brain abnormalities that are considered as part of Chiari II malformation (i.e. tectal beaking, cortical anomalies, callosal anomalies, etc) will be reported in a separate study. They were not included in this analysis as they likely represent the indirect effects of the degree of ventriculomegaly and abnormal posterior fossa, which have already been accounted for in this analysis.

Study limitations include its retrospective nature, the small sample size, and the intra- and interobserver variability in ultrasound measurement of ventricular width. Furthermore, our study limits prediction of the need for HT to the first year after birth and therefore results may vary in more advanced postnatal age. The differences in the rate of HT in our cohort (33.3%) *vs* that in the MOMS trial (40% prenatal repair; 52–91% postnatal repair[27]) likely reflect differences in pediatric neurosurgery practice and may limit generalizability of our results. Our results were not validated with an external cohort, which is a relevant next step in determining the validity of our conclusions.

The main strengths of our study are the novelty of the comprehensive evaluation of the fetal brain before and after prenatal MMC repair (using advanced imaging methods at different prenatal timepoints) and the study design with the intent of finding the best way to predict the need for postnatal HT. Including this predictive capability in individualized counseling will benefit families and providers, thereby facilitating the selection of appropriate centers for delivery and postoperative pediatric neurosurgery care.

In conclusion, we established that a detailed postsurgery *in-utero* MRI assessment of HBH 6 weeks after prenatal MMC repair independently predicts the need for postnatal HT better than prenatal ultrasound or MRI ventricular assessment alone. Secondly, we highlighted the distinct advantage of using MRI over ultrasound, as MRI provides a more effective tool for prediction. Our findings support the Unified Theory of Chiari II malformations that HBH is one of multiple factors that can cause hydrocephalus in cases of MMC[4]. Finally, accurate and early prediction of the need for postnatal HT is a critical piece in helping families receive the proper counseling and resources to choose the facility best suited for optimum neonatal and infant care and outcomes.

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## SUPPORTING INFORMATION ON THE INTERNET

The following supporting information may be found in the online version of this article:

**Figure S1** Magnetic resonance images of fetal brain obtained before surgery at 22 weeks (a–c) and after surgery at 30.2 weeks (d–f) of gestation. (a,d) Axial view of ventricle measurement before surgery (orange; a) and postsurgery (blue; d). (b,e) 3D manual segmentation volume rendering (ventricles in green) before (b) and after (e) surgery. All delineations and 3D volume reconstructions were created using Amira 6.0 software (FEI Visualization Sciences Group, Hillsboro, OR, USA). (c,f) MRI T2-weighted sequences in sagittal plane showing grade of hindbrain herniation (HBH), level of foramen magnum (line), C1 posterior arch (arrow) and lower tip of cerebellar tonsils (arrowhead) before (c) and after (f) surgery. Presurgery HBH score is 3 (c) and postsurgery HBH score is 0 (f).

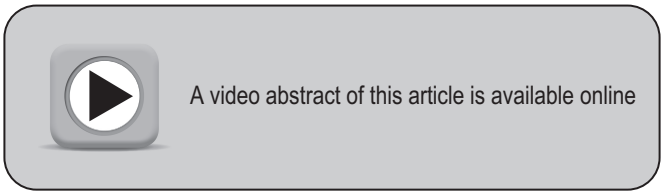
**Appendix S1** Independent variables collected from ultrasound (US) and magnetic resonance imaging (MRI) scans

**Appendix S2** MOMS trial criteria for placement of ventriculoperitoneal shunt

**Table S1** Maternal characteristics of 48 pregnancies that underwent prenatal myelomeningocele repair, according to whether they required hydrocephalus treatment during the first year postpartum

**Table S2** Surgical and perinatal data of 48 pregnancies that underwent prenatal myelomeningocele repair, according to whether they required hydrocephalus treatment during the first year postpartum

**Table S3** Predictive value of categorical variables based on MOMS trial criteria for the need of hydrocephalus treatment



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## Imágenes cerebrales prenatales para predecir el tratamiento postnatal de la hidrocefalia en fetos con reparación de defectos del tubo neural


## RESUMEN

***Objetivos*** Determinar si las imágenes cerebrales en fetos que se sometieron a reparación prenatal de defectos del tubo neural (DTN) pueden predecir la necesidad de tratamiento postnatal de la hidrocefalia (TH) en el primer año después del parto.

***Métodos*** Este fue un estudio retrospectivo de fetos diagnosticados con DTN aun abierto cuyo mielomeningocele fue reparado en el útero, entre abril de 2014 y abril de 2016. Se recolectaron variables independientes de cuatro conjuntos cronológicos de imágenes fetales: ecografía prequirúrgica, imágenes por resonancia magnética (IRM) prequirúrgica, imágenes por resonancia magnética (IRM) posquirúrgica a las seis semanas y ecografía previa al parto. Las siguientes variables independientes se recolectaron de todos los conjuntos de imágenes, a menos que se indique lo contrario: edad gestacional, perímetro cefálico, ancho ventricular medio, volumen ventricular (IRM solamente), puntaje de hernia del rombencéfalo (HR) (IRM solamente) y nivel de lesión (NDL), definido como el defecto espinal óseo superior (ecografía prequirúrgica solamente). A partir de estas mediciones se definieron y calcularon variables adicionales, como el cambio en el grado de HR, el aumento del ancho ventricular (mm/semana) y el aumento del volumen ventricular (mL/semana). La necesidad de TH (ya sea por derivación ventriculoperitoneal o por ventriculostomía endoscópica del tercer ventrículo y cauterización del plexo coroideo) fue determinada por un neurocirujano pediátrico utilizando criterios clínicos y radiográficos; se realizó un análisis secundario utilizando los criterios del estudio MOMS para la hidrocefalia. El valor predictivo de cada parámetro se evaluó mediante un análisis de la curva de la característica operativa del receptor y de la regresión logística.

***Resultados*** Se incluyeron en el estudio 50 fetos afectados, de los cuales 32 se sometieron a histerotomía abierta y 18 a reparación fetoscópica. Dos de los recién nacidos del grupo de histerotomía abierta murieron y fueron excluidos del análisis. Las edades gestacionales medias para la ecografía prequirúrgica, la IRM prequirúrgica, la IRM postoperatoria y la ecografía previa al parto fueron 21,8 ±2,1; 22,0 ±1,8; 30,4 ±1,6 y 31,0 ±4,9 semanas, respectivamente. Un total de 16 sujetos requirieron TH. El área bajo la curva (ABC) de precisión predictiva para la TH mostró que la clasificación de la HR en la IRM postoperatoria tuvo el valor predictivo más fuerte (0,86; P<0.01), por encima de otros valores predictivos como el volumen ventricular en la IRM posquirúrgica (0,73; P=0,03), el crecimiento del volumen ventricular en la IRM (0,79; P=0,01), cambios en la HR (0,82; P=0,01), y el ancho ventricular medio en la ecografía previa al parto (0,73; P=0,01). Otras variables, como el NDL, la anchura ventricular media en la ecografía prequirúrgica, la anchura ventricular media en la IRM prequirúrgica y posquirúrgica, y la evaluación del crecimiento ventricular mediante ecografía o IRM, tuvieron AUC <0,7. Para mejorar la predicción se evaluaron los límites óptimos de las variables con las AUC más altas. Los límites óptimos para la mejor predicción (razones de momios [RM], 42 [IC 95%: 4–431]; precisión, 84%) fueron una combinación de crecimiento del volumen ventricular ≥2,02 mL/semana y/o HR de 3 en la IRM postoperatoria. Los análisis de regresión logística mostraron que la persistencia de la HR grave a las 6 semanas después de la cirugía en IRM es uno de los mejores predictores de la TH (RM, 39 (IC 95%: 4–369); precisión, 84%). Los resultados no cambiaron de forma significativa cuando se utilizaron los criterios del estudio MOMS para la hidrocefalia como variable dependiente.

***Conclusiones*** La persistencia de la HR en la IRM 6 semanas después de la reparación prenatal de DTN predijo independientemente la necesidad de la TH postnatal mejor que cualquier ecografía o que otras mediciones de las características ventriculares a partir de IRM. Estos resultados deberían ayudar en el asesoramiento previo al parto y a apoyar la hipótesis de que la HR es un impulsor significativo de la hidrocefalia en pacientes con mielomeningocele.


**神经管缺损修复胎儿的产前脑成像预测产后脑积水治疗**


**摘要**

**目的：**确定神经管缺损（NTD）胎儿进行产前修复时脑成像能否预测产后第一年脑积水治疗（HT）的必要性。

**方法：**这是一个针对确诊罹患开放性神经管缺损，并在 2014 年 4 月至 2016 年 4 月之间接受宫内脊髓脊膜膨出修复的胎儿的回顾性研究。从四组按时间顺序排列的胎儿图像中收集独立变量：术前超声检查、术前磁共振成像（MRI）、6 周术后 MRI 与分娩前超声检查。从全部图像组别中收集下列独立变量，另有注释的除外：胎龄、头围、平均脑室宽度、脑室容积（对 MRI 而言）、后脑疝脱（HBH）评分（对 MRI 而言）和病变程度（LOL），定义为上骨性脊柱缺损（对术前超声检查而言）。根据这些测量值定义和计算了其他一些变量，包括 HBH 变化程度、脑室宽度增长率（毫米/周）及脑室容积增长率（毫升/周）。一位小儿神经外科医生采用临床和影像学标准确定需要 HT（通过脑室腹腔分流术或内镜第三脑室造瘘术及脉络丛烧灼），采用脑积水 MOMS 试验标准进行二次分析。通过受试者工作特征曲线和 logistic 回归分析评估每个参数的预测值。

**结果：**研究了 50 个受影响的胎儿，其中 32 人接受了开放式子宫切开术，18 人接受了胎儿镜修复术。接受开放式子宫切开术的一组中有两个新生儿死亡，没有列为分析对象。术前超声检查组、术前 MRI 组、术后 MRI 组与分娩前超声检查组的平均胎龄分别为 21.8±2.1 周、22.0±1.8 周、30.4±1.6 周和 31.0±4.9 周。总共 16 个受试者需要 HT。HT 预测精度曲线下面积（AUC）表明，术后 MRI HBH 评分的预测值是最高的（0.86; P<0.01），超过术后 MRI 脑室容积（0.73; P=0.03）、MRI 脑室容积增长率（0.79; P=0.01）、HBH 变化率（0.82; P=0.01）及分娩前超声检查平均脑室宽度（0.73; P=0.01）之类的其他预测值。LOL、术前超声检查平均脑室宽度、术前术后 MRI 平均脑室宽度、以及 MRI 或超声检查脑室增长评估之类的其他变量的 AUC 小于 0.7。评估了 AUC 最高的那几个变量的最佳临界值，以提高预测精度。脑室容积增长率≥2.02 毫升/周和/或术后 MRI 3 个 HBH 的组合是实现最佳预测的最佳临界值（比值比（OR），42 (95% CI, 4 − 431)；准确度，84%）。逻辑回归分析结果表明，MRI 检查术后 6 周持续性重度 HBH 是 HT 的最佳预测值之一（OR, 39 (95% CI, 4 − 369)；精度，84%）。将脑积水 MOMS 试验标准用作因变量时，结果基本一样。

**结论：**产前 NTD 修复后 6 周 MRI 检查持续性 HBH 独立预测出需要进行产后 HT，好于任何脑室特征的超声检查或其他 MRI 检查值。这些数值应该有助于产前咨询，也印证了这样一个假设，即 HBH 是脊髓脊膜膨出患者脑积水的重要致病因素。



 