A comparison of the accuracy of fetal MRI and prenatal ultrasonography at predicting lesion level and perinatal motor outcome in patients with myelomeningocele

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OBJECTIVE Prenatal imaging has several critical roles in the diagnosis and management of myelomeningocele, including specific family counseling and the selection of fetal surgery or postnatal repair. In this study, the authors compared the accuracy of fetal MRI and prenatal ultrasonography (US) in predicting the spinal lesion level and assessed the correlation between imaging findings and motor function as independently evaluated by a physical therapist (PT) after birth.

METHODS A retrospective review of demographic and clinical data was performed to identify children who had been treated with postnatal myelomeningocele closure at a single institution between March 2013 and December 2018. Patients were eligible for inclusion if they had all of the following: prenatal US identifying the neural tube defect level, fetal MRI identifying the neural tube defect level, and postoperative PT evaluation identifying the motor deficit level. Statistical analysis was performed using Cohen's kappa coefficient to compare the US- and MRI-demonstrated lesion level and correlate these findings with the motor level assigned postnatally by a PT via manual muscle testing.

RESULTS Thirty-four patients met the inclusion criteria. The mean gestational age at US was 23.0 ± 4.7 weeks, whereas the mean gestational age at MRI was 24.0 ± 4.1 weeks. The mean time from surgery to the PT evaluation was 2.9 ± 1.9 days. Prenatal US and MRI were in agreement within one spinal level in 74% of cases (25/34, $\kappa = 0.43$). When comparing the US-demonstrated spinal level with the PT-assigned motor level, the two were in agreement within one level in 65% of cases (22/34, $\kappa = 0.40$). When comparing MRI-demonstrated spinal level with the PT motor level, the two were in agreement within one level in 59% of cases (20/34, $\kappa = 0.37$). MRI and US were within two spinal levels of the PT evaluation in 79.4% and 85.3% of cases, respectively. MRI and US agreed within two levels in 97.1% of cases. Prenatal US and MRI were equivalent when comparing the difference between the imaged level and the postnatal motor deficit level (mean level difference: 1.12 ± 1.16 vs 1.17 ± 1.11 , $p = 0.86$).

CONCLUSIONS Prenatal US and MRI equivalently predicted the postnatal motor deficit level in children with myelomeningocele. These data may be valuable in prenatal prognostication.

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KEYWORDS myelomeningocele; spina bifida; ultrasound; magnetic resonance imaging; physical therapy

MYELOMENINGOCELE is the most common neural tube defect and congenital anomaly of the central nervous system, affecting approximately 1 neonate in 1000 live births worldwide.^{10,15} In the United States, approximately 2 neonates in every 10,000 live births will undergo surgical closure of a myelomeningocele.¹⁴ Prenatal imaging evaluation is essential in early diagnosis to accurately counsel families regarding the potential benefits of different treatment options, including fetal repair.

One component of the decision to pursue fetal surgery is understanding how this decision may impact functional outcome elements such as ambulation given the slight improvement in neurological function that fetal intervention may confer.²

For decades, prenatal transabdominal ultrasonography (US) has been the modality of choice for prenatal diagnosis of neural tube defects such as myelomeningocele, as well as other abnormalities of the central nervous sys-

ABBREVIATIONS IMMSG = International Myelodysplasia Study Group; PT = physical therapist; US = ultrasonography.

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tem.^{6,8} More recently, fetal MRI has been used in conjunction with screening US for further prenatal evaluation of myelomeningocele.^{9,13,18,20,21} Both US and MRI have demonstrated validity in terms of prenatal imaging correlation with postnatal imaging, with previous reports of approximately 60%–90% prenatal-postnatal imaging agreement.^{1,6,8,13} Prior studies have also correlated prenatal US and MRI in terms of prenatal neural tube defect level and lateral ventricle measurements in patients with myelomeningocele, finding good agreement overall.^{1,3,4,12,13,19}

To our knowledge, no study has specifically investigated the relationship between prenatal imaging and postnatal motor deficit in infants with myelomeningocele, particularly by using formal manual muscle testing performed by a physical therapist (PT). Understanding the degree of correlation between prenatal imaging and postnatal deficit would provide helpful information regarding deficit prognosis by using prenatal imaging. The goal of the current study was to evaluate the diagnostic and prognostic ability of prenatal US and MRI as they relate to postnatal motor deficit in myelomeningocele to aid in accurate and patient-specific prenatal counseling.

Methods

Patient Cohort

Institutional review board approval was granted for the study before data collection. We performed a retrospective chart review to identify children who had been treated with postnatal myelomeningocele closure in the period from March 2013 through December 2018 at Primary Children's Hospital. Patients were eligible for inclusion if they had all of the following: prenatal transabdominal US study with the corresponding spinal lesion level identified, fetal MRI study with the corresponding spinal lesion level identified, and postoperative manual muscle testing by a PT with an assigned motor level. Patients were excluded if their imaging reports were not available (with read and lesion level determination by radiology faculty at our institution), if they had been treated with fetal surgery, or if they had not undergone a documented postoperative PT evaluation within 1 week of myelomeningocele repair.

Imaging Modalities

Prenatal images were obtained solely to assess the anatomical level of the neural tube defect. Transabdominal US was the initial imaging modality for all included patients. We did not include patients in the current study if they did not have a reviewable US study before prenatal MRI. The specific ultrasound imaging equipment and technique varied by the site of imaging (ultrasound images were acquired at the University of Utah Hospital, Primary Children's Hospital, or a referring satellite clinic), but the first screening US study that was available for each patient with a diagnosis of a neural tube defect and an assigned spinal level was used for study purposes. Fetal MRI was reviewed once it had been confirmed that the patient had a prior screening US with mention of a spinal defect. All MRI was performed on a Siemens Avanto 1.5-T scanner (Siemens Medical). All images were interpreted by an attending radiologist with expertise in fetal MRI. Figure 1 displays representative fetal MRI and prenatal US studies.

FIG. 1. Representative fetal MRI (left) and prenatal US (right) studies of the same fetus demonstrating an open neural tube defect at approximately the L4 level.

Physical Therapy Evaluation

Study inclusion criteria required each patient to have a postnatal, postoperative (post-myelomeningocele closure) PT evaluation, including full manual muscle testing by a licensed PT in the inpatient setting within 1 week of surgery. Evaluations were performed by different PTs, but they all followed established guidelines specified by the International Myelodysplasia Study Group (IMSG) criteria for assigning motor levels (Table 1).^{16,23} The examination must have documented motor evaluation of the hip flexors/extensors, knee flexion/extension, and plantar flexion/dorsiflexion with corresponding assessment of functional motor level.

Statistical Analysis

Descriptive statistics including frequencies of all variables of interest were generated. Contingency tables were generated, and Cohen's kappa (κ) coefficient was calculated to correlate the US-demonstrated lesion level with the MRI-demonstrated lesion level and to correlate the postnatal PT-assigned motor level with the prenatal US and MRI spinal levels. The percent agreement within one level between the imaging modalities (US and MRI) was calculated, as was the percent agreement within one level between imaging modalities and the PT motor level. Comparisons were also made for agreement within two levels. A κ value of 0–0.4 indicates marginal agreement; 0.41–0.75, good agreement; and 0.76–1.00, excellent agreement. The absolute difference in spinal level between modalities was calculated. Continuous variables were compared using the unpaired Student t-test with a two-tailed p value. Continuous variables were reported as the mean $\pm$ standard deviation unless otherwise specified. The alpha for significance was set to 0.05. All statistical analyses were performed using IBM SPSS software version 25 (IBM Corp.).

Results

Thirty-four patients treated with postnatal myelomeningocele closure met the inclusion criteria (Table 2). There was a slight female predominance to our cohort ($n = 19$ [55.9%]). The mean gestational age at the time of US was 23.0 ± 4.7 weeks, whereas the mean gestational age at MRI was 24.0 ± 4.1 weeks. All patients were treated with postnatal myelomeningocele closure. The mean time from

TABLE 1. IMSG criteria for motor function evaluation in children with myelomeningocele

Motor Level	Functional Assessment by Muscle Group ($\geq$ grade 3 strength)*
T10	Weak lower trunk musculature, no observable lower extremity movement
T12	Quadratus lumborum (lat vertebral column flexion), no observable lower extremity movement
L2	Hip flexion, hip adduction
L3	Hip flexion, knee extension
L4	Knee extension, ankle dorsiflexion, ankle inversion
L5	Ankle dorsiflexion & inversion, knee flexion, stronger ankle plantar flexion w/ inversion (peroneus tertius)
S1	At least 2 of the following: plantar flexion, gluteus medius muscle, gluteus maximus muscle, hip stability
S2–3	All lower trunk & lower extremity muscle groups grade 5 (exception for 1 or 2 groups w/ grade 4 strength)

Based on material from McDonald et al.,¹⁷ Cameron and Monroe,⁷ and Frontera et al.¹¹

* Grade 3 = antigravity.

birth to surgery was 1.0 ± 0.5 days, and the mean time from surgery to PT evaluation was 2.9 ± 1.9 days.

Table 3 displays the anatomical distribution of the spinal defect and motor deficit level by imaging modality and PT evaluation. Figure 2 displays the relative difference in spinal level by modality. The majority of spinal defects on prenatal imaging had the upper spinal level in the lower lumbar area (70.6% and 79.4% of defects were at or below L4 for US and MRI, respectively). Half (50.0%) of the motor deficit level distribution on PT evaluation was at or below L4. However, there were more upper lumbar deficits on PT evaluation (8 patients [23.5%] with L1 or L2 level) compared with those on US (1 patient [2.9%]) and MRI (no patients). Very few thoracic lesions (1 each [2.9%] on MRI and PT evaluation) were observed.

Table 4 displays the imaging modality analysis. Prenatal US and MRI were in agreement within one spinal level in 74% of cases (25/34, $\kappa = 0.43$) and within two levels of each other in 97.1% of cases. The mean difference in spinal level between the two modalities was 0.77 ± 0.87 levels. When comparing US spinal level with PT motor deficit level, the two were in agreement within one level in 65% of cases (22/34, $\kappa = 0.40$). When comparing MRI spinal level with PT motor level, the two were in agreement within one level in 59% of cases (20/34, $\kappa = 0.37$). US and MRI levels were within two levels of the PT evaluation in 85.3% and 79.4% of cases, respectively. None of these comparisons was significantly different ($p > 0.05$). Prenatal US and MRI were equivalent when comparing the difference between the imaged level and the PT motor level (mean difference in level: 1.12 ± 1.16 vs 1.17 ± 1.11 , $p = 0.86$).

Discussion

To our knowledge, this is the first study to report an association between prenatal imaging modalities and post-

TABLE 2. General characteristics of patients treated with postnatal myelomeningocele closure

Variable	Value
Total no. of patients	34 (100%)
Sex	
M	15 (44.1%)
F	19 (55.9%)
Gestational age at US in wks	23.0 ± 4.7
Gestational age at MRI in wks	24.0 ± 4.1
Time from surgery to PT evaluation in days	2.9 ± 1.9
Postnatal closure	34 (100%)
Time from birth to surgery in days	1.0 ± 0.5

Values are expressed as number (%) or as mean $\pm$ standard deviation.

natal motor deficit by formal PT evaluation according to established criteria. Prenatal imaging has served a vital role in the diagnosis and management of myelomeningocele; however, whether prenatal imaging can reliably predict postnatal motor function remains unclear. We have shown that prenatal US and MRI are equally effective in predicting postnatal motor deficit level and are generally within one level of the postnatally observed motor deficit. Furthermore, in agreement with a small number of prior studies,^{1,13} we have demonstrated that US and MRI have good interstudy agreement regarding spinal defect level.

In our patient cohort, prenatal MRI and prenatal US agreed within one spinal level in 74% of cases with a κ of 0.43, indicating good agreement. Furthermore, the absolute difference between US and MRI was 0.77 ± 0.87 levels (mean $\pm$ standard deviation). Overall, these findings are consistent with those in prior studies. Aaronson et al.¹ compared prenatal US and prenatal MRI with postnatal spinal radiographs in patients with myelomeningocele, finding that 79% of 70 prenatal US images correlated within one level of postnatal spinal radiographs ($\kappa = 0.60$) and that 82% of 38 prenatal MRI studies correlated within one level of postnatal radiographs ($\kappa = 0.63$); these authors did not report a statistical comparison of US and MRI.

TABLE 3. Anatomical distribution of spinal defect or motor deficit level by modality

Upper Spinal Level	No. (%)		
	Prenatal US Spinal Defect Level	Prenatal MRI Spinal Defect Level	Postnatal PT Motor Deficit Level
Above T12	0 (0)	0 (0)	0 (0)
T12	0 (0)	1 (2.9)	1 (2.9)
L1	0 (0)	0 (0)	5 (14.7)
L2	1 (2.9)	0 (0)	3 (8.8)
L3	9 (26.5)	6 (17.6)	8 (23.5)
L4	5 (14.7)	7 (20.6)	7 (20.6)
L5	10 (29.4)	11 (32.4)	4 (11.8)
S1	9 (26.5)	7 (20.6)	6 (17.6)
S2 or below	0 (0)	2 (5.9)	0 (0)

FIG. 2. Relative difference in spinal level by modality (in reference to postnatal PT motor level). Each color represents one patient.

Carreras et al.⁸ published a comparison of prenatal US and postnatal neurological examination in 18 infants with myelomeningocele; they found that agreement between prenatal US and postnatal segmental levels on examination was 91.7% for the right limb ($\kappa = 0.80$) and 88.9% for the left limb ($\kappa = 0.73$). Griffiths et al.¹³ reported on agreement between fetal MRI and US with regard to general spinal deformity, finding in 40 (80%) of 50 fetuses that MRI and US were in complete agreement. Bruner et al.⁶ described a comparison of community prenatal US imaging findings with postnatal radiographs. They demonstrated that community-assigned levels agreed perfectly with postdelivery levels in 26% of cases, whereas 66% agreed within one level and 80% agreed within two levels. Collectively, these data suggest that prenatal US and MRI are equivalent overall in their ability to localize open neural tube defects.

Prior studies have investigated the utility of prenatal imaging for predicting postnatal outcome in children with myelomeningocele (Table 5). Biggio et al.⁵ published a study of 33 patients in whom the prenatal US spinal level correlated with the postnatal ambulatory status evaluated at 2 years of age or older (no prenatally observed patients with thoracic lesions were ambulatory at 2 or more years, all patients with L4–sacral lesions were ambulatory at 2 or more years, and 50% of patients with L1–3 lesions were ambulatory at 2 or more years). Chao et al.⁹ studied the associations of prenatal MRI findings with postnatal outcomes in 36 children with neural tube defects, finding that

the absence of a covering membrane on MRI was associated with postnatal scoliosis (36% vs 0% with membrane present) and with high-risk bladder dysfunction (71% vs 36%; both $p < 0.05$). These authors also observed that a higher lesion level, a larger segment span, and an interpediculate distance > 10 mm were associated with full-time wheelchair use (all three: $p < 0.05$). Van Der Vossen et al.²² reported that a higher prenatal US lesion level correlated with higher odds of death by 5 years of age, but they did not find correlates with motor functioning at 5 years of age. If prenatal imaging is indeed accurate at predicting postnatal outcome, this information could prove valuable in prenatal counseling as well as in predicting postnatal needs in light of the predicted prenatal deficit.

Study Limitations

This study has several limitations. The generalizability of our results is limited by the fact that our analysis only includes data from a single center. Furthermore, the sample size is relatively small. We only analyzed data on postnatal myelomeningocele closure; therefore, our results are potentially not applicable to patients who undergo prenatal closure. We only reported physical therapy evaluation at the postnatal, postclosure time point, meaning that the postnatal, preclosure motor deficit was not formally assessed by a PT for all infants; it would be ideal to have both preclosure and postclosure postnatal PT assessments, especially in order to evaluate any difference in the motor deficit level pre- and postoperatively. The retrospective nature of this analysis limits a more standardized approach to imaging modalities/techniques, imaging analysis methods, and timing of the prenatal imaging and postnatal PT evaluation. Images were only reviewed by the initial radiologist except in instances in which there was ambiguity in the initial radiology report. The PT evaluations were not performed by the same therapist, which could lead to interobserver variability in how the motor deficit evaluations were performed. Despite these limitations, we believe these data provide valuable insight into the predictive ability of prenatal US and MRI with regard to postnatal motor deficits in infants with myelomeningocele.

Conclusions

We present data correlating prenatal US and MRI spinal levels with postnatal motor deficits in children with myelomeningocele repaired postnatally. These modalities were equally effective at predicting the postnatal motor

TABLE 4. Imaging modality comparison with postnatal motor deficit

Variable	Prenatal MRI	Prenatal US	p Value
Agreement w/in 1 level of postnatal PT evaluation	20/34 (58.8%)	22/34 (64.7%)	0.613
Agreement w/in 2 levels of postnatal PT evaluation	27/34 (79.4%)	29/34 (85.3%)	0.527
κ statistic*	0.37	0.40	—
Mean level difference vs postnatal PT motor level ($\pm$ SD)	1.17 $\pm$ 1.11	1.12 $\pm$ 1.16	0.86

SD = standard deviation.

* For comparison of agreement within 1 level.

TABLE 5. Summary of prior literature on imaging and postnatal outcome in patients with myelomeningocele

Authors & Year	Cohort & Study Type	Findings
Comparing different imaging modalities		
Aaronson et al., 2003	Myelomeningocele patients w/ prenatal US & prenatal MRI w/ postnatal spinal radiographs (70 images)	79% of 70 prenatal US images correlated w/in 1 level of postnatal spinal radiographs ($\kappa = 0.60$) & 82% of 38 prenatal MR images correlated w/in 1 level of postnatal radiographs ($\kappa = 0.63$)
Bruner et al., 2004	Consecutive cases of spina bifida repaired in utero w/ comparison of prenatal US w/ postnatal radiography (171 cases)	US agreed perfectly w/ postnatal radiographs in 26% of cases, 66% agreed w/in 1 level, & 80% agreed w/in 2 levels
Carreras et al., 2016	Prenatal US & postnatal neurological examination in infants w/ myelomeningocele (18 infants)	Agreement btwn prenatal US & postnatal segmental levels on examination was 91.7% for rt limb ($\kappa = 0.80$) & 88.9% for lt limb ($\kappa = 0.73$)
Griffiths et al., 2006	Patients w/ fetal US & MRI w/ general spinal deformity (50 fetuses)	In 40 (80%) of 50 fetuses, MRI & US imaging were in complete agreement regarding level & pathology of deformity
Prenatal imaging predicting postnatal outcome		
Biggio et al., 2001	Patients w/ prenatal US & postnatal ambulatory status evaluated at ≥ 2 yrs of age (33 patients)	Prenatal US spinal level correlated w/ postnatal ambulatory status (no prenatally observed patients w/ thoracic lesions were ambulatory at ≥ 2 yrs, all patients w/ L4–sacral lesions were ambulatory at ≥ 2 yrs, & 50% of patients w/ L1–3 lesions were ambulatory at ≥ 2 yrs)
Chao et al., 2011	Prenatal MRI findings associated w/ postnatal outcomes in children w/ neural tube defects (36 patients)	Higher prenatal lesion level, larger segment span, & interpediculate distance >10 mm were associated w/ full-time wheelchair use (all 3: $p < 0.05$)
Van Der Vossen et al., 2009	Prenatal US examinations of live-born children who were prenatally diagnosed w/ spina bifida (41 cases)	Higher prenatal US lesion level correlated w/ higher odds of death by 5 yrs of age, but no correlation w/ motor functioning at 5 yrs of age

deficit level and were generally within one level of the postnatally observed motor deficit. These data may be helpful in prenatal prognostication.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Bollo, Ho. Acquisition of data: Sherrod, Ho. Analysis and interpretation of data: Sherrod, Ho. Drafting the article: Bollo, Sherrod, Ho, Hedlund. Critically revising the article: Bollo, Sherrod, Ho, Kennedy, Ostrander. Reviewed submitted version of manuscript: Bollo, Sherrod, Ho. Approved the final version of the manuscript on behalf of all authors: Bollo.

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