Fetal MRI improves diagnostic accuracy in patients referred to a fetal center for suspected esophageal atresia

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Purpose: The purpose of this study was to describe prenatal imaging characteristics and outcomes of fetuses with suspected esophageal atresia (EA) in order to improve prenatal diagnosis, counseling, and management.

Methods: The medical records of all patients referred to our multidisciplinary fetal center for suspected EA from January 2003 to April 2013 were reviewed retrospectively.

Results: Thirty-three patients were referred with a prenatal diagnosis of possible EA. Following fetal center evaluation with MRI, EA was deemed unlikely in 6 (18%) fetuses. Of 27 fetuses in whom EA could not be excluded, EA was confirmed postnatally in 15 (56%), excluded in 7 (26%), and unconfirmed in 5 (3 fetal losses; 2 lost to follow-up). Imaging characteristics on fetal MRI associated with the highest positive predictive values (PPV) were an esophageal pouch (100%) and a small stomach (75%). The finding of polyhydramnios had high sensitivity (93%) but low specificity (31%) and PPV (61%) for a diagnosis of EA.

Conclusion: Prenatal imaging and fetal center evaluation correctly identify the presence or absence of esophageal atresia in 78% of patients referred on suspicion of this condition. The presence of an esophageal pouch on fetal MRI has significant predictive value for EA. These data may assist with evidence-based prenatal family counseling.

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Accuracy in the prenatal diagnosis of esophageal atresia (EA) is elusive; despite recent improvements in prenatal imaging, the antenatal detection rate remains less than 50% [1–4]. Because the normal esophagus is often not seen on routine ultrasound examination [5], suspicion for EA is raised indirectly in the presence of polyhydramnios or a small or absent stomach bubble [1]. In isolation, these findings are not specific for detecting EA, as both are associated with a variety of different, more commonly encountered conditions [2,6,7]. Combining the findings of a small or absent stomach bubble and polyhydramnios might slightly improve the positive predictive value of EA detection [4,6,8]. For those fetuses with multiple anomalies the prenatal diagnosis of EA is complicated even further, and false positive rates are as high as 78% [3] in these patients.

In an effort to improve antenatal diagnostic capabilities in this disease, recent focus has been placed on the identification of an esophageal pouch, or a ‘pouch sign’. Caused by dilatation of the blind-ending upper esophageal segment during fetal swallowing, it is considered to be the most consistent indicator of EA on prenatal imaging with a reported positive predictive value as high as 100% [9,10]. However, detection of the pouch sign on ultrasound can be difficult, as it depends on fetal position, mobility, gestational age, and active fetal swallowing during the exam [7,10,11].

The aim of this study was to describe the prenatal imaging characteristics and outcomes of fetuses with suspected esophageal atresia referred to a comprehensive, multidisciplinary fetal center in order to improve prenatal diagnosis, counseling, and management.

1. Methods

All patients referred to our center underwent a comprehensive ultrasound examination at the initial visit, and most patients had fetal MRI. Those patients with no other indication for fetal MRI and normal amniotic fluid and stomach bubble on radiology-performed ultrasound at the time of fetal center consultation had no other imaging. MRI scans were performed without sedation or contrast as primarily T2-weighted single shot and balanced steady-state free precession sequences. In a typical case, serial sagittal images at a single level in the midline were obtained more than 20 second intervals to evaluate fetal swallowing and the transient distension of the proximal esophagus. Imaging assessment focused on identifying polyhydramnios, the presence and size of the stomach, esophageal anatomy, the presence of a dilated esophageal pouch (Fig. 1), and evidence of other
associated anomalies. Patients with no evidence of esophageal abnormality or only polyhydramnios on comprehensive ultrasound or MRI imaging were assigned a negative prenatal screen for EA. Patients with abnormal imaging were suspected of having EA until delivery. Postdelivery EA was confirmed based on findings on chest radiograph and at surgery, or ruled-out based on successful passage of a nasogastric tube into the stomach.

Following approval from the institutional review board of Baylor College of Medicine (protocol # H-29695), we reviewed the medical records and diagnostic imaging studies of all fetuses referred to the Texas Children’s Fetal Center between January 1, 2003 and April 30, 2013 with a suspected diagnosis of EA. Suspicion for esophageal atresia was based on the referral diagnosis described by each patient’s independent obstetrician. Data collected included gestational age at initial fetal center imaging and consultation, results of imaging studies, postconsult diagnosis, postnatal diagnosis, and perinatal outcomes. Patients were classified as being negative EA (prenatally), negative EA (postnatally), and positive EA. We compared negative EA to positive EA patients with respect to patient data and imaging characteristics. Data were analyzed using chi-square and Student’s t-test.

2. Results

2.1. Initial presentation

Thirty-three patients were referred to our center prenatally for suspected EA during the study period (Fig. 2). Twenty-eight (85%) patients underwent comprehensive ultrasound and fetal MRI scans, while 5 (15%) had only comprehensive ultrasound examination. The mean gestational age at the time of fetal center imaging and evaluation was 30.2 ± 4.5 (18.4–37.4) weeks. On ultrasound, 22 (76%) patients had polyhydramnios (mean AFI 28.63 ± 9.11) and 20 (61%) had a small or absent stomach bubble. On MRI, 11 (39%) patients had a pouch sign while in 10 (36%) there was incomplete visualization of the esophagus. Patients were classified as being negative EA (prenatally), negative EA (postnatally), and positive EA. We compared negative EA to positive EA patients with respect to patient data and imaging characteristics. Data were analyzed using chi-square and Student’s t-test.

2.2. Prenatal diagnosis

Following evaluation, EA was deemed unlikely in 6 (18%) fetuses. Five of the 6 had both ultrasound and MRI scans at a mean GA of 31.98 ± 4.34 (range, 26.29–37.43) weeks. Four of the 6 (67%) had polyhydramnios (median AFI 25.45), but none had a small or absent stomach bubble. On MRI, none had a pouch sign or incomplete visualization of the esophagus. In 4 of the 6, other anomalies were detected—3 had findings suggestive of Trisomy 21, and 1 had a neural tube defect with tethered cord.

In 27 (82%) patients, a diagnosis of EA could not be excluded. Twenty-three of the 27 had both ultrasound and MRI scans at a mean GA of 29.8 ± 4.52 weeks. Twenty-one (78%) of the 27 had polyhydramnios (median AFI 29, range 8.1–41) and 19 (70%) had a small or absent stomach bubble. On MRI, 11 (49%) had a pouch sign, while 10 (43%) had incomplete visualization of the esophagus. Fourteen (52%) patients had other significant anomalies on prenatal imaging.

2.3. Postnatal diagnosis and perinatal outcomes

Of the 27 fetuses in which EA could not be excluded prenatally, EA was confirmed postnatally in 15 (56%) (Table 1). Of those confirmed

![Fig. 1. Sagittal view of dilated esophageal pouch on fetal MRI, 31 weeks gestation.](image)

![Fig. 2. Flow chart of patients referred for evaluation of possible EA.](image)

Seven patients (21%) had a constellation of findings suggestive of VACTERL association, and 5 had findings suggestive of Trisomy 21.

### Table 1

Patient characteristics and imaging findings in patients with prenatal referral for suspected esophageal atresia.

<table>
<thead>
<tr>
<th></th>
<th>Confirmed EA (n = 27)</th>
<th>No EA (n = 20)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>M/F</td>
<td>14/13</td>
<td>6/14</td>
<td>0.45</td>
</tr>
<tr>
<td>GA at prenatal imaging, weeks</td>
<td>31.69 ± 3.2</td>
<td>31.69 ± 3.2</td>
<td>0.45</td>
</tr>
<tr>
<td>Imaging findings</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Polyhydramnios</td>
<td>14 (93%)</td>
<td>8 (67%)</td>
<td>0.14</td>
</tr>
<tr>
<td>Small stomach bubble</td>
<td>12 (80%)</td>
<td>4 (33%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Pouch sign on MRI</td>
<td>10/12 (83%)</td>
<td>0/10 (0%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Incomplete visualization of esophagus on MRI</td>
<td>6/12 (50%)</td>
<td>2/10 (20%)</td>
<td>0.2</td>
</tr>
<tr>
<td>Other significant anomalies on prenatal imaging</td>
<td>9 (60%)</td>
<td>8 (67%)</td>
<td>1.00</td>
</tr>
<tr>
<td>GA at birth, weeks</td>
<td>36.5 ± 2.3</td>
<td>37.3 ± 2.3</td>
<td>0.41</td>
</tr>
<tr>
<td>Birth weight, grams</td>
<td>2390 ± 474.3</td>
<td>3124.7 ± 507.3</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Abbreviations: EA, esophageal atresia; GA, gestational age.
cases, 12 (73%) had both comprehensive ultrasound and fetal MRI scans as part of our fetal center evaluation at a mean gestational age of 30.42 ± 4.97 weeks. Fourteen (93%) of the 15 had polyhydramnios scans as part of our fetal center evaluation at a mean gestational age of 31.28 ± 3.14 (range, 26.29–39.29) weeks, with an average birth weight of 2390 ± 474 (range, 3820–3827) grams.

Thirteen (39%) patients did not have EA. Of those, a diagnosis of EA was thought unlikely in 6 (46%) following prenatal evaluation, while in 7 (54%) EA could not be excluded prenatally. Of those 13 patients, 11 (85%) had both comprehensive ultrasound and fetal MRI scans at a mean gestational age of 31.28 ± 3.14 (range, 26.29–37.43) weeks. Nine (69%) of the 13 had polyhydramnios (median AFI 26.8, range 11.8–41), and 4 (31%) had a small or absent stomach bubble. On MRI, none of the 11 had a pouch sign, while 2 (18%) had incomplete visualization of the esophagus. Other significant anomalies were detected on prenatal imaging in 9 (60%) cases—1 had complex cardiac defects, 2 had duodenal atresia, 5 had findings suggestive of VACTERL, and 1 had Trisomy 21. Among the confirmed EA group, the average GA at birth was 36.54 ± 2.25 (range, 33.29–40.14) weeks, with an average birth weight of 3820 ± 474 (range, 3280–3827) grams.

In 5 five patients no postnatal diagnosis could be confirmed—two pregnancies were electively terminated following evaluation, 1 suffered intrauterine fetal demise at approximately 36 weeks gestation, and 2 were lost to follow-up.

### 2.4. Diagnostic value of prenatal imaging

Overall, polyhydramnios was 93% sensitive and 31% specific, with a positive predictive value (PPV) of 61%, and a negative predictive value (NPV) of 80% (Table 2). A small or absent stomach bubble was 80% sensitive and 69% specific, with a PPV of 75% and NPV of 75%. A pouch sign on MRI was 83% sensitive and 100% specific, with a PPV of 100% and NPV of 85%. Incomplete visualization of the esophagus on MRI was 50% sensitive and 82% specific, with a PPV of 31% and NPV of 61%.

### Table 2

<table>
<thead>
<tr>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polyhydramnios</td>
<td>93%</td>
<td>31%</td>
<td>61%</td>
</tr>
<tr>
<td>Small stomach bubble</td>
<td>80%</td>
<td>60%</td>
<td>75%</td>
</tr>
<tr>
<td>Pouch sign on MRI</td>
<td>83%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Incomplete visualization of esophagus on MRI</td>
<td>50%</td>
<td>82%</td>
<td>75%</td>
</tr>
</tbody>
</table>

Abbreviations: PPV, positive predictive values; NPV, negative predictive values.

The prenatal diagnosis of EA often depends on indirect imaging findings such as a small or absent stomach bubble or polyhydramnios. The clinical variability in etiology for these indirect signs leads to high false positive rates and missed diagnoses [2,8]. The identification of a pouch sign and the use of fetal MRI have both been suggested to improve diagnostic accuracy [4,6,9], though large cohort studies detailing the effectiveness of either fetal MRI or the pouch sign are lacking [12,13].

In the present study, we identified 33 patients who were referred to our fetal center for suspected EA. Following evaluation, EA was deemed unlikely in 6 (18%) fetuses because of a lack of radiologic evidence suggestive of the disease and none of these patients were found to have EA postnatally. In 27 fetuses the diagnosis of EA could not be excluded. While EA was thought to be more likely in some than others at the time of evaluation, no standardized reporting terminology was used at the time to risk-stratify the radiologist’s impression. Postnatally, 15 patients were confirmed to have EA, while 13 were confirmed not to have the disease. Of the 5 patients in whom a postnatal diagnosis could not be confirmed, multiple congenital anomalies were identified on prenatal imaging and EA was thought likely in all cases. If we consider only those cases in which the final pathology is known, our diagnostic accuracy is 78%.

Polyhydramnios showed the highest sensitivity (93%) in our study, and was present in 14 of the 15 patients with confirmed EA. The patient who did not have polyhydramnios had, instead, a low

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**Fig. 3.** Coronal view of an enlarged stomach and dilated distal esophageal pouch in two cases (a and b) with esophageal atresia and duodenal atresia on fetal MRI. Arrows indicate the dilated distal esophageal segments, which are distended in these cases because of the closed-loop obstructions at either end.
An intrathoracic esophagus [4]. Similarly, we found a 100% specificity of cases of congenital anomalies accounting for only 10% to 20% of cases [6] and EA accounting for only 1% of causes [7]. Thus, it was not surprising that the specificity of polyhydramnios in our study was low (31%).

A small or absent stomach bubble was present in 12 of the 15 patients with confirmed EA, resulting in a sensitivity of 80%. Of note, 2 of the confirmed EA patients who did not have a small stomach had concomitant duodenal atresia, which resulted in an enlarged stomach in both cases (Fig. 3), and the third had EA associated with a distal tracheoesophageal fistula (TEF). While our sensitivity is lower than in other studies [2], the positive predictive value of a small or absent stomach bubble (75%) was higher than previous reports of 44–56% [1,8]. The combined positive predictive value of polyhydramnios plus a small or absent stomach bubble was 85%, which is also improved compared to other reports [1,3,4,8]. The findings seen in the present study may be specific to fetal center referral patterns. Most patients have been screened with previous fetal ultrasound studies prior to referral. Also, those with additional anomalies besides simply polyhydramnios or a small stomach may be more likely to be referred.

A dilated esophageal pouch sign was seen in 83% of our patients with confirmed EA who had a fetal MRI. Brantberg et al. found only 43% of their 21 prenatally diagnosed EA patients with pouch sign visualization, and only 1 had a pouch sign in a study of 10 patients by Langer et al. [2,4]. However, these studies, only reported the visualization of the pouch sign using ultrasonography. One case report by Salomon et al. describes two patients with polyhydramnios and a small stomach who were prenatally diagnosed with EA based on the visualization of an esophageal pouch on MRI [12]. Data on the pouch sign on both comprehensive ultrasound and MRI are limited and deserve further investigation [6,15].

The use of MRI to diagnose EA prenatally is promising. Matsuoka et al. diagnosed EA in a single case based on the dilatation of the hypopharynx [13], and Langer et al. reported 100% sensitivity, 80% specificity, and 83% positive predictive value using MRI to diagnose 5 cases of confirmed EA based on the nonvisualization of the intrathoracic esophagus [4]. Similarly, we found a 100% specificity and 100% positive predictive value using MRI to diagnose EA based on the identification of an esophageal pouch. Continued efforts to improve the accuracy of prenatal detection of EA are important for both medical and nonmedical purposes. Patients with EA often have multiple concomitant anomalies and require care at a tertiary children's hospital to facilitate immediate access to neonatal surgical services and other subspecialty care. Furthermore, parents benefit from prenatal counseling with prognostic information specific to their child's disease process, and directed, optimal perinatal care. As has been shown, accurate prenatal counseling may prepare the family for a potentially long and rocky postnatal hospitalization and increase satisfaction with their child's care [7].

While there are still technical and financial limitations to the regular use of MRI, our success in correctly identifying the presence or absence of EA in 78% of patients, which is enhanced by detecting a dilated esophageal pouch, suggests that MRI is a promising tool for the evaluation of fetuses with suspected EA. Though this study is the largest to describe the role of fetal MRI in the evaluation of fetuses with suspected EA, it remains limited by small patient numbers and retrospective design. Future efforts will focus on combining these data with the experience from other centers for external validation, and educating referring obstetricians on the clinical significance of pertinent ultrasound findings, as well as the potential benefits of fetal MRI.

References