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# Dynamic esophageal patency assessment: an effective method for prenatally diagnosing esophageal atresia

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**BACKGROUND:** Esophageal atresia is a major anomaly with a low prenatal detection rate. We propose a sonographic method termed dynamic esophageal patency assessment.

**OBJECTIVE:** This study aimed to assess the feasibility and performance of the dynamic esophageal patency assessment in a high-risk population. **STUDY DESIGN:** A prospective study was conducted in a single tertiary fetal ultrasound unit for 12 months. The study group included pregnant women referred for a targeted scan because of one or more of the following: (1) polyhydramnios; (2) small or absent stomach; (3) vertebral, anal atresia, cardiac, tracheoesophageal fistula, renal, and limb abnormalities; (4) firstdegree relative with esophageal atresia; and (5) genetic mutation associated with esophageal atresia. In addition to dynamic esophageal patency assessment, a comprehensive anomaly scan was carried out. The fetal esophagus was observed during swallowing. Cases that demonstrated uninterrupted fluid propagation through the esophagus were classified as normal. Cases that demonstrated interrupted fluid propagation, with the formation of a pouch, were classified as abnormal. Cases with unclear visualization of the esophagus or cases that failed to demonstrate either fluid propagation or a pouch were classified as undetermined. Dynamic esophageal patency assessment results were compared with postnatal findings, considered "gold standard." Test performance indices and intra- and interobserver agreements were calculated.

**RESULTS:** For 12 months, 130 patients were recruited, and 132 fetuses were scanned. The median gestational age (interquartile range) at the time of scan was 31.4 weeks (29.0-35.3). Of 132 fetuses enrolled, 123 (93.2%) were normal, 8 (6%) were abnormal, and 1 (0.8%) was undetermined. Excluded from test performance analysis were 3 cases that were terminated without postmortem autopsy (1 was abnormal and 2 were normal), and a fourth case was excluded as it was classified as undetermined. The detection rate of esophageal atresia was 100%, with no false-positive or false-negative case. Sensitivity, specificity, and positive and negative predictive values of the dynamic esophageal patency assessment were 100%. The Kappa coefficient was 1 for both inter- and intraobserver agreements (P<.0001). The median time (interquartile range) required to complete the dynamic esophageal patency assessment was 6.00 minutes (3.00-13.25).

**CONCLUSION:** The dynamic esophageal patency assessment is a feasible and highly effective method of ascertaining an intact esophagus and detecting esophageal atresia in suspected cases.

**Key words:** absent stomach, esophageal atresia, esophageal pouch, fetal swallowing, polyhydramnios, prenatal diagnosis, small stomach, tracheoesophageal fistula

#### Introduction

In many cases, esophageal atresia (EA) with or without tracheoesophageal fistula is a major anomaly, requiring corrective surgery and postrepair interventions. Despite treatment, this condition often leads to chronic gastrointestinal and respiratory sequelae.<sup>1-6</sup> EA carries an 8% mortality rate, especially among neonates with a low birthweight or a coexisting cardiac anomaly.<sup>5</sup>

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Click <u>Video</u> under article title in Contents at **ajog.org**  Its prevalence is estimated to be 1 in 2500 to 3800 live births.<sup>7–10</sup> Unfortunately, the prenatal detection rate of EA with or without tracheoesophageal fistula is relatively low, reported to be around 30% in multiple studies.<sup>7,11–16</sup> Consequently, timely prenatal consultation, psychological preparation, and the option of pregnancy termination are precluded. Currently, there is no validated prenatal systematic method to confirm an intact esophagus. Several earlier studies have described various methods of demonstrating the fetal esophagus at rest, but these were descriptive studies and were not designed to assess test performance for the detection of EA.<sup>17–20</sup>

We proposed a dynamic esophageal patency assessment (DEPA) based on either the demonstration of a continuous amniotic fluid wave propagating through the fetal esophagus or the accumulation of fluid in an esophageal pouch during swallowing. This study aimed to examine the feasibility, performance, and characteristics of DEPA in a population at risk of EA with or without tracheoesophageal fistula.

#### Methods

A prospective study was conducted at a single tertiary fetal ultrasound unit for 12 months. Singleton or multiple pregnancies were included and referred for a targeted scan because of the following: (1) polyhydramnios (as defined by the referring center); (2) small or absent stomach (as defined by the referring center); (3) vertebral, anal atresia, cardiac, tracheoesophageal, renal, and limb (VACTERL) abnormalities; (4) positive first-degree family history of EA; or (5) genetic mutation associated with EA

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A patent

#### AJOG at a Glance

#### Why was this study conducted?

This prospective study was conducted to evaluate the performance of a method aiming to prenatally determine esophageal patency.

#### **Key findings**

The proposed method accurately detected all cases of fetal esophageal atresia (EA) while confirming an intact esophagus in all healthy cases. High intra- and interobserver agreements were achieved. A detailed description of the method's technique has been provided.

#### What does this add to what is known?

The currently used sonographic signs of EA result in a 30% prenatal detection rate. Based on a dynamic scan of the esophagus, the proposed method has a high detection rate with high positive and negative predictive values.

with or without tracheoesophageal fistula. A comprehensive anomaly scan was carried out complemented by the investigational DEPA supplement. Scans were performed by 4 operators (E.K., T.W., E.H., and B.M.) with varying experience in DEPA acquisition, 1 operator with 10 years of DEPA experience and the remaining 3 operators having performed 5 DEPA scans, before the onset of the study.

# Dynamic esophageal patency assessment

The fetal esophagus was observed during swallowing, and patency was confirmed when a continuous fluid wave propagated through the esophagus in at least 1 of 2 segments: (1) from the hypopharynx to the level of the tracheal bifurcation and (2) from the level of the aortic arch to the diaphragm. Evidence supporting the choice of these 2 segments to determine esophageal continuity is provided in the DEPA technique principles section below. In these cases, EA was ruled out, and this was classified as DEPA normal (Figure 1, A; Supplemental Video 1). Cases that demonstrated an esophageal pouch during swallowing were classified as DEPA abnormal (Figure 1, B; Supplemental Video 2). Cases with unclear visualization of the esophagus or those that failed to demonstrate either fluid propagation, in at least 1 segment, or a pouch were classified as DEPA undetermined. DEPA results were compared with esophageal patency as



**A**, DEPA normal. The esophagus, marked by *arrows*, appears distended with sonolucent fluid, located behind the trachea and heart. **B**, DEPA abnormal. An esophageal pouch, marked by *arrows*, is apparent in the lower neck or upper chest area during swallowing. *DEPA*, dynamic esophageal patency assessment.

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esophagus was confirmed in neonates discharged after normal feeding was documented. EA was diagnosed in suspected cases (either prenatally suspected or postnatally because of frequent regurgitation) on gastric tube instilled contrast media x-ray showing a blind esophagus. This was confirmed during corrective surgery. Cases that underwent pregnancy termination were confirmed by postmortem autopsy. Excluded from test performance analysis were DEPA undetermined cases and terminated pregnancies without a postmortem autopsy (Figure 2). The test performance measures evaluated included sensitivity, specificity, and negative and positive predictive values (NPV and PPV), along with various examination characteristics. Intra- and interobserver agreements for the interpretation of DEPA clips were assessed as follows: 50 original DEPA study clips, including 44 DEPA negative and 6 DEPA abnormal, were reviewed in a blinded and random fashion. Half of the clips were performed by operator 1 (E.K.) and half by operator 2 (T.W.). DEPA classification as determined during this blinded review by operator 1 was compared with the DEPA classification as originally determined by operators 1 and 2, during the live DEPA scan.

postnatally.

determined

To further study the feasibility of the method, a comparison between experienced and inexperienced operators was performed.

# Dynamic esophageal patency assessment technique principles

Several technical principles need to be addressed: sonographic landmarks, the course of the esophagus, the ideal fetal lie, the esophageal segment needed to be demonstrated, and technique adaptation in unfavorable fetal lie.

# The course of the esophagus and sonographic landmarks

The esophagus is a collapsed fibromuscular tube with its rostral end located posterior to the cricoid cartilage of the trachea. It descends through the neck and upper chest, posterior to the trachea and anterior to the fetal spine

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(Supplemental Figure, A). The esophagus has a unique appearance on ultrasound at rest. It appears as a longitudinal bundle of echogenic stripes (Figure 3). The trachea serves as a prominent landmark when scanning the esophagus. Contrary to the collapsed esophagus, it is easily discernible as a fluid-filled tubular structure in the fetal neck and upper chest (Figure 4). At the level of the tracheal bifurcation, the esophagus begins to change its course. It gradually crosses the midline, over the descending aorta, toward the left, coursing anteriorly, to come in direct contact with the posterior wall of the left atrium before traversing the diaphragm (Figure 5).<sup>21</sup> Fluid propagation through the fetal esophagus is exhibited in Figure 1, A, and Supplemental Video 1. Recognizing the characteristic sonographic appearance and anatomic route of the collapsed fetal esophagus assists in DEPA demonstration, especially in challenging cases.

A naturally occurring indentation of the esophagus is exerted by the aortic arch and left main bronchus as it crosses over the midline (Figure 6).<sup>21</sup> This esophageal constriction is apparent when fluid passes through the esophagus (Figure 7; Supplemental Video 3).

# The ideal dynamic esophageal patency assessment plane

To demonstrate the whole length of the esophagus, the ideal fetal position is supine ("spine down"), with the fetal neck in a neutral or extended position. Initially, the focus is placed on the trachea. After acquiring this plane, the operator should try to visualize the subtle appearance of the collapsed esophagus (Figure 5). If the fetal neck is flexed, the upper esophagus and trachea are often obscured by acoustic shadows cast by the bony skull, maxilla, and mandible.

#### Dynamic esophageal patency assessment adaptation to spine-up or spine-side positions

In contrast to the spine-down position, which enables the demonstration of the whole esophagus in 1 shot, the spine-up and spine-side positions render a segmented view, in either a posterior



DEPA, dynamic esophageal patency assessment.

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The collapsed esophagus, marked by *arrows*, appears as a longitudinal bundle of fibers of varying echogenicity. It courses posterior to the trachea and anterior to the spine and descending aorta. *Kassif et al. An effective method for prenatally diagnosing esophageal atresia. Am J Obstet Gynecol 2021.* 

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#### FIGURE 4 The fetal trachea



The fetal trachea, marked by *arrows*, serves as a prominent landmark of the adjacent esophagus. *Kassif et al. An effective method for prenatally diagnosing esophageal atresia. Am J Obstet Gynecol 2021.* 



The esophagus courses behind the trachea until the level of bifurcation and below the aortic arch, where it crosses over the descending aorta and courses anteriorly, to come in direct contact with the posterior wall of the left atrium before traversing the diaphragm. Reprinted from Drak et al.<sup>21</sup> *Kassif et al. An effective method for prenatally diagnosing esophageal atresia. Am J Obstet Gynecol 2021.* 

parasagittal plane (Figure 8, A; Supplemental Video 4) or a coronal plane (Figure 8, B; Supplemental Video 5; Supplemental Figure 1, B). Because of the segmented demonstration of the esophagus, these planes should be reserved for persistent spine-up and spine-side fetal positions.

# Esophageal segment involved in esophageal atresia

The DEPA definition of an intact esophagus relies on the expected locations of the pouch and gap of the missing esophagus. Apart from rare variants, pouches are usually located above the aortic arch and fistulas, usually connected to the carina when present.<sup>22-24</sup> The gap in the esophagus is located between the pouch and distal esophageal stump. Therefore, if fluid is seen propagating from the level of the neck and slightly past the aortic arch, then a pouch is safely ruled out (Figure 9, A). In addition, if fluid is seen propagating from the level of the aortic arch down to the diaphragm, then a gap is ruled out (Figure 9, B). Ideally, the whole length of the esophagus should be demonstrated. However, it is sufficient to demonstrate either one of these segments, to safely rule out EA with or without tracheoesophageal fistula.

#### **Data retrieval**

Prospective data were collected at the time of the scan using a designated case report form completed by the investigators. This included patient demographic data, medical history, prenatal care, and real-time DEPA scan parameters, such as the fetal lie, the amniotic fluid index, the number of scans needed, and the time needed to complete DEPA.

Postnatally, we reviewed neonatal medical records for postnatal conditions, including EA with or without tracheoesophageal fistula. A patent esophagus was determined in neonates discharged after normal feeding was documented. EA was diagnosed on x-ray imaging using gastric tube instilled contrast media, showing a blind esophagus. In cases of EA, surgery reports were reviewed to ascertain the type of EA. Patients that delivered at other centers

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A naturally occurring indentation of the esophagus is exerted by the aortic arch and left main bronchus as it crosses over the midline. Reprinted from Drak et al.<sup>21</sup>

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were contacted and asked to provide hospital discharge letters.

The study protocol was approved by the institutional ethics committee (approval number 5344-18-SMC). Informed consent was obtained from all participating patients.

#### **Statistical analysis**

Normality of the data was tested using the Shapiro-Wilk or Kolmogorov-Smirnov tests. Data are presented as median and interquartile range (IQR). Comparison between unrelated ordinal variables was conducted with the

Student t test or Mann-Whitney U test, as appropriate. The chi-square and Fisher exact tests were used for comparison among categorical variables. Significance was accepted at a *P* value of <.05. Test performance measures (sensitivity, specificity, NPV, and PPV) were calculated using a contingency table. The Cohen Kappa was calculated for intra- and interobserver agreements. Level of agreement was defined according to the Kappa result, as previously described by Landis and Koch<sup>25</sup>: poor (0.00-0.20), fair (0.21-0.40), moderate (0.41-0.60), good (0.61-0.80), and perfect (0.81–1.00). Statistical analyses were conducted using the IBM Statistical Package for the Social Sciences (version 23; IBM Corporation Inc, Armonk, NY).

#### Results

Between September 2019 and August 2020, 130 pregnancies with 132 fetuses met the inclusion criteria and were enrolled and scanned for DEPA. Descriptive details of the DEPA scan are exhibited in Table 1. Of 132 fetuses enrolled, 123 (93.2%) were classified as DEPA normal, 8 (6%) were classified as DEPA abnormal, and 1 (0.8%) was classified as DEPA undetermined. Moreover, 4 cases were excluded from test performance analysis but included in feasibility calculation. These included 3 cases that underwent termination of pregnancy without a postmortem autopsy and 1 DEPA undetermined case (Figure 2). Of the 3 terminated cases, 1 was DEPA abnormal and was consequently terminated for this reason. The other 2 cases were DEPA normal and were terminated for other congenital anomalies. The undetermined case was postnatally found to have an intact esophagus.

# Dynamic esophageal patency assessment test characteristics

Various test characteristics are presented in Table 1. Nearly 24% of fetuses were scanned in a nonideal position (spine up or spine side). Approximately 20% of cases required 2 scans until DEPA was completed. Most of the cases were scanned during the third trimester of

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#### FIGURE 7

Esophageal narrowing near the aortic arch



Pressure exerted by the aortic arch and left main bronchus causes a natural esophageal constriction. This indentation can be noticed as fluid passes through the esophagus.

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pregnancy (median, 31.4 weeks [IQR, 29.0–35.3 weeks]). It took a median time of 6 minutes (IQR, 3.00–13.25 minutes) from the beginning of the first DEPA trial to completion. It took a median time of 36 minutes (IQR, 14–72 minutes) from the beginning of the scan to DEPA completion. Moreover, three-quarters of the patients had a body

mass index (BMI) below 27 before pregnancy.

#### **Test performance**

Test performance measures were calculated using a contingency table (Table 2), comparing the DEPA result (normal or abnormal) with the postnatal diagnosis (EA or patent esophagus). The

#### FIGURE 8

Swallowing in coronal and posterior sagittal views



**A**, Swallowing in coronal view. The distended esophagus, marked by *arrows*, is located adjacent to the carotid artery. **B**, Swallowing with a pouch in posterior sagittal view. The esophageal pouch is located anterior to the spine and posterior to the trachea.

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sensitivity of DEPA was 100% (7 of 7 cases), with no false-positive or falsenegative case. Hence, specificity, PPV, and NPV of DEPA were all 100%. Feasibility reached 99.2%, with 1 case undetermined because of failure to demonstrate the esophagus on 2 separate attempts. Of note, the patient was scanned by an inexperienced operator, the fetus was in a spine-up position on both occasions, and the patient's BMI was 39.3. The patient subsequently refused further scans.

#### Intra- and interobserver agreement

The intra- and interobserver agreements are displayed in Tables 3 and 4. There was complete agreement (Kappa 1, P<.0001) between the index interpretation and revised interpretation of the DEPA scan by operator 1. In addition, there was complete agreement on DEPA interpretation between operators 1 and 2.

#### **Operator experience**

A comparison of DEPA characteristics between experienced and inexperienced scanners is presented in Table 5. Most of the scans were performed by inexperienced operators, 76 vs 56 scans (Table 3). There was no statistically significant difference among the groups in the rate of multiple pregnancies, degree of polyhydramnios, gestational age at the time of scan, or patient BMI. DEPA was completed in a shorter time and more often in 1 scan, when performed by the experienced operator (P=.06 and .07, respectively). The only DEPA undetermined case was scanned twice by an inexperienced operator, with the fetus in a persistently nonideal position along with a patient with high BMI (39.3). There was a similar rate of DEPA abnormal cases (EA) in both groups (37.5% vs 62.5%; P=.28). DEPA performance measures were equally unexceptionable in both groups.

#### Comment

This study suggested that DEPA accurately detects EA with excellent performance, even in less experienced operators. This is a significant improvement compared with previous reports of

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#### **FIGURE 9** DEPA normal required segments



A, Upper segment. Fluid is seen propagating from the neck and past the arch. The ascending aorta is marked by a single arrow. B, Lower segment. Fluid is seen propagating from the aortic arch and down. Arrows on the left point to the trachea. Arrows on the right point to the lower distended esophagus. The aortic arch is marked by a star.

DEPA, dynamic esophageal patency assessment.

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detection to 30% prenatal up rate.<sup>9,11,13,16,26-29</sup> DEPA was shown to have high intra- and interobserver agreements, suggesting that the interpretation of the method is straightforward. Moreover, one of the leading

advantages of DEPA is its ability to confirm an intact esophagus, sparing the need for repeated scans and costly magnetic resonance imaging (MRI) scans. The most prominent disadvantage of this method is its time consumption, with 16.7% of cases lasting over 20 minutes and 19.7% of cases requiring 2 scans. This may necessitate longer scan appointments and, occasionally, multiple scans.

Earlier studies have investigated the appearance of the fetal esophagus on prenatal ultrasound. Moreover, one of the earliest studies was a study by Avni et al<sup>30</sup> published in 1994. In this study, 155 patients were scanned in either the second or third trimester of pregnancy. The appearance of the esophagus was described as multiple parallel echogenic lines and was divided into 3 segments: cervical, thoracic, and abdominal. The

#### TABLE 1

#### DEPA test characteristics and background descriptives of the study group

| DEPA characteristics                       |  | N=132               |                           |
|--|--|---------------------|---------------------------|
| Multiple pregnancies, %                    |  | 6.9% (9/130)        |                           |
| Indication for DEPA scan                   | Indication for scan                                    | Study group (N=132) | DEPA abnormal cases (n=8) |
|  | Isolated polyhydramnios                                | 74.2% (98/132)      | 25.0% (2/8)               |
|  | Small or absent stomach with or without polyhydramnios | 15.9% (21/132)      | 75.0% (6/8)               |
|  | VACTERL  | 7.6% (10/132)       | _                         |
|  | Familial esophageal atresia                            | 1.5% (2/132)        |                           |
|  | Genetic mutation associated with esophageal atresia    | 0.8% (1/132)        | _                         |
| Patient BMI (kg/m <sup>2</sup> )           |  | 23.4 (20.8–26.8)    |                           |
| Patient BMI (kg/m <sup>2</sup> ), range    |  | (13.4—45.0)         |                           |
| Gestational age at examination (wk)        |  | 31.4 (29.0-35.3)    |                           |
| Spine up or spine side                     |  | 23.8% (31/130)      |                           |
| DEPA completed in >1 scan                  |  | 19.7% (26/132)      |                           |
| Minutes from scan start to DEPA completion |  | 36 (14-72)          |                           |
| Minutes from DEPA start to completion      |  | 6 (3.00–13.25)      |                           |
| DEPA result                                | Abnormal   | 6.0% (8/132)        |                           |
|  | Normal   | 93.2% (123/132)     |                           |
|  | Undetermined   | 0.8% (1/132)        |                           |

BMI, body mass index; DEPA, dynamic esophageal patency assessment; VACTERL, vertebral, anal atresia, cardiac, tracheoesophageal, renal, and limb abnormalities. Kassif et al. An effective method for prenatally diagnosing esophageal atresia. Am J Obstet Gynecol 2021.

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sonographic appearance of the fetal esophagus in a low-risk population. None attempted to determine esophageal patency or continuity. Moreover, 2 additional descriptive studies included sporadic examples of EA with or without tracheoesophageal fistula. Dall'asta et al<sup>19</sup> described 3D imaging of the esophagus on Crystal Vue rendering technology and assessed its feasibility in 89 normal fetuses and in 2 fetuses with suspected EA. This method relied on volume acquisition in a supine fetal position and offline post-

processing resulting in a 3D image of the esophagus showing its continuity. In cases of suspected EA, discontinua-

tion of the esophagus was discernible.

Feasibility of the method reached 83%

with unfavorable lie and acoustic

shadows impairing visualization in

17% of cases. Postnatally, the 2 EA

cases and the remaining intact esoph-

agus cases were confirmed. Test per-

formance was not assessed. Develay-

Morice et al<sup>20</sup> published an article in

French describing a 2D assessment of a

thoracic region they referred to as

"sensitive" for EA.<sup>20</sup> The region

described was the course of the

esophagus between the descending

aorta and trachea. Normally, the

descending aorta and trachea are

separated by the esophagus. In 1 case of

EA with tracheoesophageal fistula in

this study, the aorta seemed to come in

direct contact with the trachea without

a discernable separating esophagus.

Distal to this region, the esophagus

reappeared and seemed connected to

the trachea, consistent with a trache-

oesophageal fistula. Collectively, this group of articles describes the course and appearance of the fetal esophagus on prenatal ultrasound in the normal population, along with some anecdotal cases of EA. The sonographic appearance and course of the esophagus in these studies were similar to the current study. The report by Develay-Morice et al<sup>20</sup> supports our argument that the region between the aortic arch and carina is the most crucial for determining esophageal continuity, as this is where the gap in the esophagus

will be found, in EA. Unlike our study,

| DEPA test performance   |                                       |                                       |       |
|---|---------------------------------------|---------------------------------------|-------|
| Cases with postnatal or<br>postmortem esophageal<br>assessment (n=128) <sup>a</sup> | Postnatal patent<br>esophagus (n=121) | Postnatal esophageal<br>atresia (n=7) | Total |
| DEPA abnormal (n=7)   | 0% (0/7)                              | 100% (7/7)                            | 7     |
| DEPA normal (n=121)   | 100% (121/121)                        | 0% (0/121)                            | 121   |
|   | 121                                   | 7                                     | 128   |

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rate of visualization of each segment throughout pregnancy was assessed. The thoracic segment was found to be most frequently visualized. Fetal swallowing with fluid propagation was incidentally recorded in one-third of patients. It was noted that color Doppler did not appear during fluid passage. This was attributed to the slow velocity of flow during swallowing. A similar descriptive study was conducted by Malinger et al.<sup>17</sup> Esophageal anatomy and peristaltic patterns were assessed on ultrasound in 60 low-risk patients at the midtrimester of pregnancy. As in the pioneering study by Avni et al,<sup>30</sup> the rate of visualization of the 3 esophageal segments was evaluated. Visualizing the entire length of the esophagus was feasible in 87% of patients and at least part of the esophagus in 97% of patients. The cervical, thoracic, and abdominal segments were similarly demonstrated in 90% to 93% of cases. Visualization of the esophagus was

found to be impaired by maternal obesity but not by fetal lie. This is contrary to our findings that suggested that both maternal obesity and unfavorable fetal lie impair the demonstration of the whole length of the esophagus. This difference probably stems from the fact that, unlike the study by Malinger et al,<sup>17</sup> most patients were scanned during the third trimester of pregnancy, when acoustic shadows cast by fetal bones are more prominent. Another large study by Venkatesh<sup>18</sup> evaluated the visualization of the collapsed esophagus in the first, second, and third trimesters of pregnancy. This was one of the first studies to address the esophagus in the first trimester of pregnancy. The demonstration rate of the cervical esophageal segment was slightly lower in the first trimester of pregnancy, but overall, at least 1 segment was visualized in all cases throughout pregnancy. All 3 studies were descriptive reports of the

| TABLE 3           DEPA intraobserver agreement |          |   |  |  |
|--|----------|---|--|--|
| Observation                                    |          | Operator 1 index result   |  |  |
|  |          | Normal  | Total  |  |
| Abnormal                                       | 3        | 0   | 3  |  |
| Normal   | 0        | 22  | 22   |  |
|  | 3        | 22  | 25   |  |
|  | Abnormal | Operator 1 ind       Abnormal       Abnormal       Normal       0 | Operator 1 index resultAbnormalNormalAbnormal30Normal022 |  |

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none of these studies systematically assessed their methods in a high-risk population to evaluate test performance.

The only definitive prenatal diagnostic sign of EA is an esophageal pouch, which was first reported antenatally in 1983 by Eyheremendy et al.<sup>31</sup> Since then, it has been described in several case series.<sup>32–37</sup> This sign demonstrated a 100% PPV and NPV in diagnosing EA in a small study of 25 patients.<sup>35</sup> Subsequent studies reported a low detection rate of up to 30%.<sup>7,9,13,16,26-29</sup> These studies were retrospective and regarded the pouch as a sonographic sign that may or may not appear, without trying to actively demonstrate its formation. Unlike the DEPA method, none provided a method of confirming an intact esophagus. To further improve the prenatal detection of EA, additional modalities were suggested, such as MRI and amniotic fluid analysis.<sup>12,37–40</sup> Although providing some added value, none displayed substantial improvement in the

| TABL | E 4           |           |
|------|---------------|-----------|
| DEPA | interobserver | agreement |

|                           |          | Operator 2 index result |        |       |
|---------------------------|----------|-------------------------|--------|-------|
| Observation               |          | Abnormal                | Normal | Total |
| Operator 1 blinded review | Abnormal | 3                       | 0      | 3     |
|                           | Normal   | 0                       | 22     | 22    |
|                           |          | 3                       | 22     | 25    |

DEPA, dynamic esophageal patency assessment.

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detection of EA. MRI showed several advantages compared with ultrasound: it is less operator dependent and not affected by fetal lie, maternal obesity, or acoustic shadows. However, its major limitation, apart from cost and availability, was that it required that the fetus swallow during the examination; otherwise, patency could not be addressed. Studies that have assessed MRI performance were retrospective and affected by selection bias, with the most suspicious cases referred. A sensitivity of 66.7% to 100.00%, specificity of 46.15 to 100.00%, and feasibility of 47.6% to 100.00% were reported.<sup>12,13,16,29,37,38</sup>

#### Strengths and weaknesses

This study presented a method for determining fetal esophageal integrity. Supported by test performance analysis, the method was shown to be highly effective for prenatally ruling out esophageal atresia. The study included a relatively large number of normal and EA

| DEPA characteristics                       | Experienced (n $=$ 56) | Inexperienced (n=76) | <i>P</i> value   |
|--|------------------------|----------------------|------------------|
| Multiple pregnancies                       | 5.4% (3/56)            | 7.9% (6/76)          | .29              |
| Degree of hydramnios <sup>a</sup>          |                        |                      |                  |
| Normal                                     | 39.3% (22/56)          | 44.7% (34/76)        | .82              |
| Mild                                       | 44.6% (25/56)          | 40.8% (31/76)        |                  |
| Moderate-Severe                            | 16.1% (9/56)           | 14.5% (11/76)        |                  |
| Patient body mass index                    | 23.7 (21.30-26.70)     | 23.0 (20.45-27.30)   | .78              |
| Gestational age at examination (wk)        | 31.5 (29—36.1)         | 31.4 (28.4–35.1)     | .57              |
| DEPA completed in $>1$ scan                | 12.5% (7/56)           | 25.0% (19/76)        | .07 <sup>b</sup> |
| Whole esophagus demonstration              | 80.4% (41/51)          | 75.3% (55/73)        | .5               |
| Minutes from scan start to DEPA completion | 28.0 (9.80-68.00)      | 45.0 (17.00-80.00)   | .06 <sup>b</sup> |
| Minutes from DEPA start to completion      | 4.0 (2.00-8.00)        | 10.0 (4.00—19.00)    | .1               |
| DEPA result                                |                        |                      |                  |
| Abnormal                                   | 8.9% (5/56)            | 3.9% (3/76)          | .28              |
| Normal                                     | 91.1% (51/56)          | 94.7% (72/76)        |                  |
| Undetermined                               | 0%                     | 1.4% (1/76)          |                  |

Data are presented as percentage (number/total number) or median (interquartile range).

DEPA, dynamic esophageal patency assessment.

<sup>a</sup> Degree of hydramnios by amniotic fluid index: normal is ≥5 cm and <24 cm; mild is ≥24 cm and <30 cm; moderate to severe is ≥30 cm; <sup>b</sup> Borderline significance (P=.05–.09). Kassif et al. An effective method for prenatally diagnosing esophageal atresia. Am J Obstet Gynecol 2021.

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with or without tracheoesophageal fistula cases to address DEPA performance. Furthermore, multiple DEPA scan parameters were recorded, providing detailed technique characterization.

There are several notable limitations of our study. The study was conducted in a single facility. The setting of the study was in a tertiary referral center, which might not represent conditions provided at community-based centers. Therefore, we refrained from deducing broad conclusions in settings that may lack appropriate resources and experience, needed for DEPA performance. The study was limited by its relatively small sample size. Because of the rarity of this condition, only 8 cases of DEPA abnormal cases were detected, of which 7 were confirmed as EA. A larger cohort with more abnormal cases would strengthen the statistical power of the study. A further limitation of the study was that it included cases with at least 1 risk factor for EA (polyhydramnios, small or absent stomach, a VACTERL sequence anomaly, etc.). Cases without a risk factor would not have been suspected for EA and therefore may be missed prenatally. To prenatally detect all cases of EA with or without tracheoesophageal fistula, DEPA should be performed in the whole parturient population, and this may not be costeffective considering the rarity of this anomaly and the time required to complete the test. In addition, most patients in our study had a prepregnancy BMI below 27. As obesity might impair the ability to demonstrate the fetal esophagus, this could affect the feasibility and performance of the DEPA method when applied in a more obese population. Nevertheless, our cohort did include patients with a BMI of up to 45, indicating that it is feasible despite obesity.

#### Conclusion

DEPA is a feasible and highly effective method of ascertaining an intact esophagus and detecting EA in suspected cases. This method has demonstrated excellent performance and intra- and interobserver agreements, regardless of operator experience.

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