

Characterization of Esophageal Motility Following Esophageal Atresia Repair Using High-Resolution Esophageal Manometry

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ABSTRACT

Background: Esophageal dysmotility, a considerable issue following esophageal atresia (EA) repair, has been reported but has not been precisely described and characterized. Using high-resolution esophageal manometry (HREM), we characterized the esophageal motility patterns in children with repaired EA and compared these patterns of dysmotility with symptomatology.

Methods: HREM was performed as an outpatient procedure in patients with repaired EA. The tracings were analyzed using the software provided by the company and were then reviewed visually. Charts were reviewed for medical/surgical histories and symptoms were assessed by a standardized questionnaire.

Results: Forty patients (25 boys, 15 girls) with a median age of 8 years (11 months–18 years) underwent an HREM. Thirty-five patients had type C EA and 5 had type A EA. Only 7 patients were asymptomatic at the time of the examination. HREM results were abnormal in all of the patients. Three different esophageal motility patterns were derived from HREM tracing analysis: aperistalsis (15 patients, 38%), pressurization (6 patients, 15%), and distal contractions (19 patients, 47%). Distal contractions pattern was found exclusively in type C EA. Dysphagia was encountered in the 3 groups. Gastroesophageal reflux disease-related symptoms predominated in the aperistalsis group.

Conclusions: HREM improves our understanding and allows precise characterization of esophageal dysmotility in patients who have undergone EA repair.

Key Words: aperistalsis, children, esophageal atresia, esophageal motility, high-resolution esophageal manometry, pressurization

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Esophageal atresia (EA) is the most common significant esophageal malformation, with an incidence of 1 in 3500 live births (1). A total of 80% to 85% of patients are affected by type C EA, with a proximal esophageal pouch and a distal tracheoesophageal fistula (TEF), whereas type A or “pure” EA without TEF is encountered in approximately 10% of patients (2). Since the first successful primary repair in 1941, postoperative outcomes have changed. With the exception of patients experiencing severe concomitant cardiac anomalies, improvements in operative and perioperative care issues evolved from mortality to morbidity and quality-of-life issues (3).

Symptoms related to esophageal dysmotility such as gastroesophageal reflux disease (GERD) and dysphagia affect up to 75% to 100% of patients with EA (4–7) and constitute the most prevalent issues in the long-term follow-up (7). It has been hypothesized that the dysmotility could contribute to dysphagia, to the high incidence of fundoplication failure in patients with EA, and to the development of esophagitis and associated complications (6).

Esophageal dysmotility has been demonstrated in children with EA using standard manometry and/or esophageal impedance but has been poorly characterized (8–10). High-resolution esophageal manometry (HREM) has revolutionized the study of esophageal motility by using greatly resolved pressure topography plots that facilitate localizing and tracking focal areas of high pressure, allowing the visualization of esophageal contractility in terms of functionally characterized components (11,12). HREM has already provided relevant information regarding esophageal motility in the adult population (13) and to a lesser extent in children (14–16). Study of esophageal motility with HREM has never been reported in patients with repaired EA.

In the present study, we studied, using HREM, esophageal motility in 40 children with repaired EA. Our aim was to precisely describe and characterize esophageal motility in such patients and to determine whether a correlation could be established between symptoms and motor patterns.

METHODS

Patient Selection and Data Collection

All patients with EA who underwent an HREM study in 3 teaching pediatric hospitals (Centre Hospitalier Universitaire Sainte-Justine [Montréal, Canada], Montreal Children’s Hospital [Montréal, Canada], and Centre Hospitalier Universitaire

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Mère-Enfants [Nantes, France]) were recruited. Agreement to be part of a multicentric database of patients with EA was obtained through the consent of each child's parents or primary caregiver. A chart review was conducted and the following data were collected: demographic (sex, date of birth), medical history (type of EA, presence/absence of TEF, long-gap defect, and associated malformations), surgical history (postoperative complications, other significant surgical procedures such as fundoplication), gastrointestinal (GI) investigations before HREM, and observed abnormalities (ambulatory 24-hour esophageal pH monitoring, upper GI endoscopy).

Symptomatology at the time of HREM (upper GI symptoms, alimentary behavior changes, and their effect on life) was evaluated through a self-assessment questionnaire systematically completed by the child or his primary caregiver. Data related to HREM were also collected (age at the time of HREM, reason to perform the examination, number of swallows performed, and technical difficulties encountered while performing the examination).

HREM Technique

HREM was performed in an outpatient setting after a 4-hour fast. The procedure was conducted without sedation in all of the patients, with the child placed in supine position. Two different sizes of catheters were used (36 channels with 12 pressure sensing points/channel, each channel 1 cm apart) (Sierra Scientific Instruments, Los Angeles, CA), according to the age and height of the patient (outside diameter of 2.75 and 4.2 mm). The catheter was inserted transnasally until the most distal recording site was positioned in the stomach. Time was allowed for the patient to calm down with the catheter in place. Once the tracing was stabilized, stomach, diaphragm, lower esophageal sphincter (LES), and upper esophageal sphincter (UES) positions were determined. Water boluses (5.0 mL for patients older than 5 years, and 2.0 mL for patients younger than 5 years) were administered by syringe every 30 seconds. Ten wet swallows were theoretically obtained depending on the capacity and collaboration of the patient.

HREM Analysis

Normative data were derived using the HREM Manoscan 360 circumferential solid-state catheter and the Manoview Analysis software version 2.0.1 (Sierra Scientific Instruments). Pressure data were acquired and shown using software designed for high-resolution manometry. All of the tracings were reviewed and analyzed by a general surgery resident (C.L.) under the supervision of a pediatric gastroenterologist (C.F.) and a pediatric surgeon (A.A.) blinded to the clinical condition and symptoms.

Swallowing was determined by pharyngeal contraction, followed by the UES relaxation. LES tone and relaxation were then evaluated; mean residual pressure and 3 seconds of integrated relaxation pressure (IRP) of the LES following swallowing and basal pressure were also measured. Esophageal length corresponded to the distance between both esophageal sphincters. The dominant characteristics of the esophageal contraction after swallows were described after generating isobaric contour plots at a 30-mmHg threshold pressure, which has been demonstrated to be the minimum pressure associated with complete bolus transit (17). Patients were classified according to their main peristaltic propagation pattern according to previously published classifications (14,17).

In patients showing evidence of peristaltic propagation, even if weak or abnormal, the following characterization was conducted: proximal and distal troughs were identified. Using an isobaric

contour line at 30 mmHg, the distance between the distal end of the proximal esophageal contractile segments and the proximal end of the distal esophageal contractile segments (the transition zone [TZ]) was measured; the distal contractile integral (DCI) and contraction front velocity (CFV) were both determined using the Manoview analysis software. DCI was then adjusted for esophageal length (distal contractile integral adjusted for esophageal length [DCIa]) (14). These data were compared with the only available pediatric reference HREM values obtained in 15 children tested for dysphagia with normal peristaltic pattern (14).

Statistical Analysis

Summary data are expressed as means (\pm standard deviation) of normally distributed data and medians (25th–75th percentile) for non-normally distributed data. *n*-Values represent the number of subjects included in the dataset. A one-way analysis of variance (ANOVA) (Kruskal-Wallis) with a Dunn post-hoc test was used to compare UES and LES values in the 3 groups of patients after peristalsis classification. Significance is expressed at the $P < 0.05$ level.

RESULTS

Patients

Forty patients took part in this study and all of them underwent HREM. Twenty-nine patients were recruited at the Centre Hospitalier Universitaire (CHU) Sainte-Justine, 4 patients at the Montreal Children's Hospital, and 7 patients at the CHU Mère-Enfants. Twenty-five patients (66%) were boys. Thirty-five patients (87%) had type C EA, whereas 5 (13%) had type A EA. Six patients (16%) (type A EA, $n = 4$; type C EA, $n = 2$) had a long-gap defect. Fourteen patients also experienced other malformations: VACTERL (vertebral, anorectal, cardiac, tracheoesophageal, renal or limb defects) syndrome ($n = 6$), cardiac malformation ($n = 8$), and GI malformation ($n = 7$). Surgery-related data are shown in Table 1.

Twenty-one patients had an esophagogastroduodenoscopy that demonstrated esophageal stenosis in 5 patients and biopsy-proven esophagitis in 5 other patients. Thirteen patients underwent an ambulatory 24-hour pH monitoring before the manometry. GER was demonstrated in 5 patients.

Systematic GER- and dysphagia-related symptoms evaluation at the time of the HREM is provided in Table 2. Seven of the 40 patients were asymptomatic.

TABLE 1. Surgical history of the 40 patients with EA

Surgical history	EA type	
	A ($n = 5$)	C ($n = 35$)
Postoperative complications		
Anastomotic leak	2	3
Early anastomotic stenosis	1	1
Other surgical interventions		
Nissen fundoplication	3	8
Toupet fundoplication	0	3
Anastomotic stenosis		
Occurrence	3	11
Pneumatic dilation required	3	10
Dilation <1 year from HREM	1	2

EA = esophageal atresia; HREM = high-resolution esophageal manometry.

TABLE 2. Symptoms of the 40 patients with EA

Symptoms	All patients (%)
Asymptomatic (no complaint)	7 (18)
GER (n = 15)	
Pyrosis	6 (15)
Regurgitation	8 (20)
Heartburn	6 (15)
Nausea	7 (18)
Vomiting	5 (12.5)
Obstructive (n = 18)	
Blockage sensation	12 (30)
Dysphagia	
Liquids	1 (2.5)
Thickened liquids	2 (6)
Soft foods	5 (12.5)
Dry foods	11 (28)
Solids	14 (35)
Change in alimentary habits (n = 29)	
Need to drink	17 (43)
Change in diet	20 (50)
Last to finish meal	13 (33)
Pulmonary (cough, pneumonia)	15 (37.5)

GER = gastroesophageal reflux.

Esophageal Motility

HREM was performed at a median age of 8 years (11 months–18 years). The test was ordered as an evaluation of esophageal motility in 36 patients. Four patients underwent the study for concomitant placement of the pH monitoring probe. Most studies were performed without technical difficulties. Thirty-three patients were able to complete ≥ 10 swallows. Of the 7 remaining, 4 could only perform ≤ 7 swallows, with 1 patient unable to complete >4 swallows.

No patients included in this study exhibited a normal peristaltic pattern (Fig. 1). When visually analyzing HREM tracings, 3 different esophageal motility patterns were identified: complete aperistalsis, pressurization, and distal esophageal contraction.

Patients with a complete aperistalsis pattern showed a complete lack of esophageal body motility, with or without LES anomalies (Fig. 1B). Fifteen patients (38%) demonstrated this aperistalsis pattern.

Pressurization pattern was identified when contraction of the entire esophageal body was observed following UES relaxation (Fig. 1C). Six patients (15%) were found to have this pressurization motility pattern. All of these patients had a panesophageal pressurization.

Distal esophageal contraction was defined as the presence of esophageal middle third (Fig. 1E) and/or distal third (Fig. 1D) contraction after deglutition in at least 2 swallows and was identified in 19 patients (47%). Discernible continuous isobaric contour at the 30-mmHg threshold pressure was absent in all 19 patients

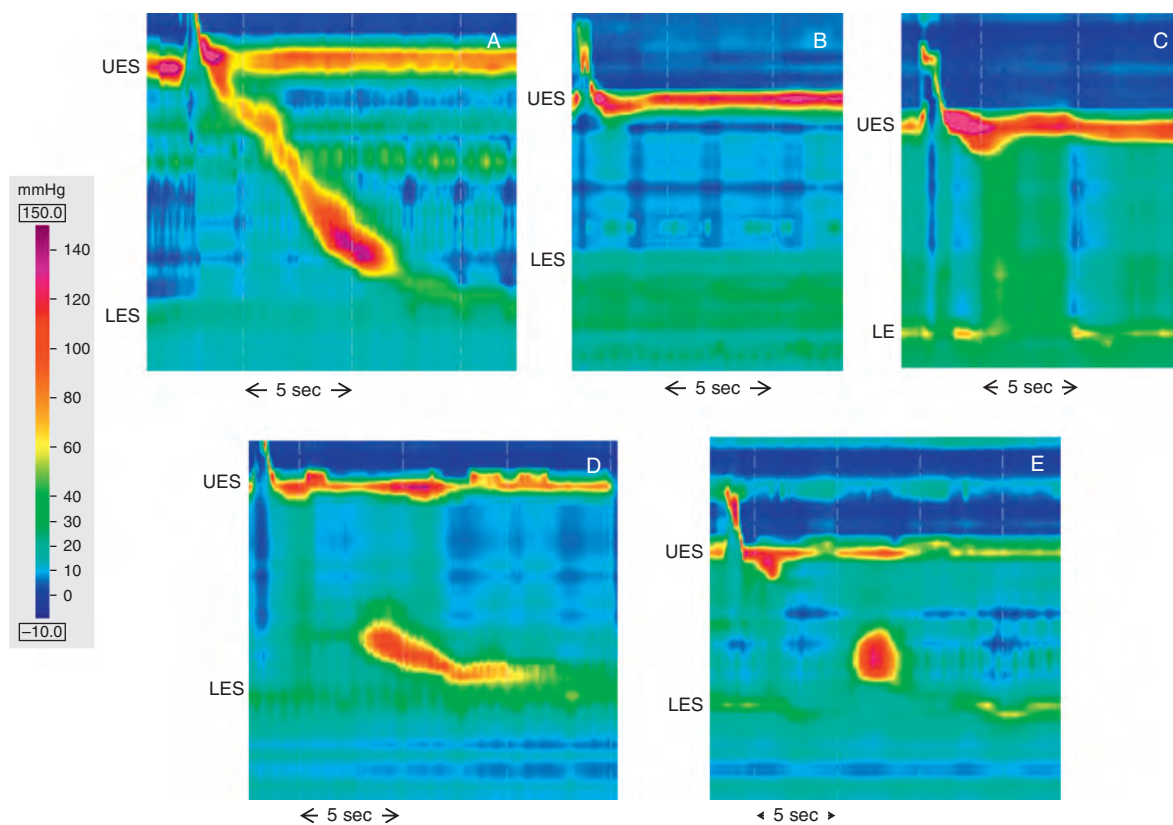


FIGURE 1. A, Normal peristalsis tracing. B, Aperistalsis pattern. C, Pressurization pattern. D–E, Various types of distal contraction pattern (D, middle and distal third, continuous; E, middle third). Pressure scale is shown on the left part of the figure. Time scale is shown under each manometry tracing. LES = lower esophageal sphincter; UES = upper esophageal sphincter.

TABLE 3. HREM-derived variables and peristalsis classification

HREM results	Peristalsis classification		
	Aperistalsis (n = 15)	Pressurization (n = 6)	Distal contraction (n = 19)
UES			
Residual pressure (<12 mmHg)	7.9 mmHg (−5.2 to 11.8)	6.2 mmHg (0–16.6)	5.9 mmHg (3.3–13.5)
LES			
Basal pressure (15–31 mmHg)	7.8 mmHg (5.6–15.4)	19.9 mmHg (2.4–51.5)	30.5 mmHg* (18.6–36.3)
No. hypertonic (>32 mmHg) (%)	1 (7)	1 (17)	9 (47)
No. hypotonic (<8 mmHg) (%)	7 (47)	2 (33)	2 (11)
IRP (<15 mmHg)	3.5 mmHg (2.2–8.9)	7.8 mmHg (0.1–22.4)	12.2 mmHg (4.3–14.5)
# Normal IRP values (%)	14 (93)	5 (83)	11 (58)
Esophageal body			
DCI (2311–3149 mmHg/cm/s)	—	—	302 mmHg/cm/s (72–437)
DCIa (161–259 mmHg/s)	—	—	13.4 mmHg/s (3.4–23.1)
CFV (2.5–4.1 cm/s)	—	—	1.6 cm/s (−8 to 5.6)
Transition zone	—	—	7.6 cm (6.3–9.6)

CFV = contraction front velocity; DCI = distal contractile integral; DCIa = distal contractile integral adjusted to esophageal length; HREM = high-resolution esophageal manometry; IRP = integrated relaxation pressure; LES = low esophageal sphincter; UES = upper esophageal sphincter. Data are expressed as median and ranges. Normal reference values (25th–75th percentiles) are from Goldani et al (14). No normal values of transition zone are available in children.

* $P < 0.02$ versus “Aperistalsis”; nonsignificant versus “Pressurization.”

with this distal esophageal contraction motility pattern. Isolated middle third esophageal contraction was characterized by increased proximal and distal trough (Fig. 1E) and was present in 15 patients. Distal third contraction (Fig. 1D) was present in 4 patients.

Esophageal motility was further characterized as shown in Table 3. Median UES residual pressure was similar and normal for the 3 groups. Median LES basal pressure showed more variation between groups. The lowest value (median 7.8 mmHg) was found in the aperistalsis group. Pressurization and distal contraction groups showed normal values (respectively, 19.9 and 30.5 mmHg). LES pressure was significantly lower in the aperistalsis group as compared with the distal contraction group ($P < 0.02$). TZ, DCI, DCIa, and CFV were calculated in the distal contraction group only. Median DCI, DCIa, and CFV were all low when compared with pediatric reference values (14). TZ was wider than normal adult values. In 4 patients CFV had a negative value, indicating a lack of antegrade propagation of the esophageal contractions (Fig. 1E).

GI Symptoms According to Peristalsis Classification

Data related to symptomatology and peristalsis classification are presented in Table 4. The 7 asymptomatic patients were distributed in the 3 motility pattern groups. In the 33 remaining

patients, symptoms of GER, including pyrosis, heartburn, regurgitation, and vomiting as well as obstructive symptoms and respiratory symptoms, were similarly reported regardless of the motility pattern.

Surgical Data According to Peristalsis Classification

All of the patients included in the distal contraction group had type C EA. Patients included in the aperistalsis and pressurization groups were the patients with the most severe malformations, namely patients with type A EA and long-gap defects. None of these patients were found in the distal contraction group (Table 5).

Eight of the 15 patients (57%) of the aperistalsis group and 4 of 6 patients (66%) of the pressurization group had undergone an antireflux procedure as compared with only 2 of 19 (14%) in the distal contraction group. Esophagitis was found both in the aperistalsis and pressurization groups.

DISCUSSION

So far, esophageal motility study in patients with repaired EA has been conducted using perfused catheters. Because of the limitations inherent to this manometry technique, it has only been possible to roughly demonstrate, in the majority of patients, a lack

TABLE 4. Symptoms according to peristalsis classification

Symptoms	Peristalsis classification (%)		
	Aperistalsis	Pressurization	Distal contraction
Asymptomatic (n = 7)	4 (57)	1 (14)	2 (29)
GER symptoms (n = 15)	6 (40)	4 (27)	5 (33)
Obstructive symptoms (n = 18)	4 (22)	4 (22)	10 (56)
Change in alimentary habits (n = 29)	9 (31)	4 (14)	16 (55)
Pulmonary symptoms (n = 15)	7 (47)	4 (27)	3 (20)

GER = gastroesophageal reflux.

TABLE 5. EA, surgical, and endoscopic data and peristalsis classification

EA-related data	Peristalsis classification (%)		
	Aperistalsis (n = 15)	Pressurization (n = 6)	Distal contraction (n = 19)
EA type			
A (n = 5)	3 (60)	2 (40)	0
C (n = 35)	12 (34)	4 (11)	19 (54)
Long-gap defect (n = 6)	4 (67)	2 (33)	0
Postoperative complications			
Anastomotic leak (n = 6)	4 (67)	1 (16)	1 (16)
Early anastomotic stenosis (n = 3)	1 (33)	2 (66)	0
Late anastomotic stenosis (n = 14)	4 (29)	4 (29)	6 (42)
Pneumatic dilations required (n = 13)	4 (31)	4 (31)	5 (38)
Other surgeries			
Fundoplication (n = 14)	8 (57)	4 (29)	2 (14)
Esophagitis (n = 7)	4 (57)	3 (43)	0
Upper GI endoscopy			
Stenosis (n = 5)	2 (40)	2 (40)	1 (20)

EA = esophageal atresia; GI = gastrointestinal.

of coordination of low-amplitude peristalsis or no peristaltic wave (6,9,18–22). Taking advantage of the advances provided by HREM, this study constitutes the first report of an all-EA pediatric patient cohort with precise evaluation and characterization of esophageal motility.

A normal esophageal peristalsis pattern in adults is composed of 3 pressure segments separated by 2 lower pressure troughs (23). This same sequence is also observed in children and young infants, including preterm neonates (15,16). The present study led to the identification of 3 different peristaltic patterns in children who were operated on for EA: complete aperistalsis (no peristaltic wave identified on all 10 swallows), pressurization (simultaneous contraction of the entire body length following deglutition associated with esophago-gastric junction relaxation), and distal contraction with evidence of middle third or distal third esophageal contraction.

Distal contraction pattern, found in 19 patients with type C EA, made possible the calculation of parameters to quantify esophageal motility. Compared with the only pediatric HREM references values available (14), median DCI and DCIa values were, as expected, abnormally low in this group, representing either an abnormal innervation and/or smooth musculature of the distal esophagus, or an abnormally short distal peristaltic esophagus or both. Whether a low value for DCI and DCIa indicates a weak peristalsis has not been demonstrated. In this group, the proximal and distal troughs were identified, demonstrating that the majority of the patients (15/19) are characterized by isolated middle third esophageal contractions (with increased proximal and distal trough; Fig. 1E). The length of the proximal trough, otherwise called “transition zone,” has not been yet characterized or quantified in the pediatric population, but in the adult population it is hypothesized that it could contribute to the occurrence of dysphagia through incomplete bolus transit (24). Adult patients with a TZ >5 cm experience more often from dysphagia. In the patients with EA with “distal contraction,” median TZ was 7.6 cm and the shortest TZ was 4.5 cm. If a TZ >5 cm in adults can be associated with symptomatology, one can suppose that a long TZ in a child (shorter esophageal body) must have symptomatic repercussions.

Pressurization pattern was found either in type A or type C EA patients. This motility pattern illustrates the lack of an organized peristalsis and represents neuropathic discordination of longitudinal and circular muscle contraction. Four of 6 patients with the pressurization pattern had previously undergone an antireflux procedure.

Fundoplication, by creating a distal obstacle through which the abnormal esophageal body should struggle, may play a role in the pressurization process; however, it should be noted that mean LES pressure and LES relaxation in these patients were similar to the other groups and were in normal ranges, suggesting that the pressurization process may be present before fundoplication, although pre- and postoperative manometric studies have not been yet conducted.

Aperistalsis was noted when no peristalsis was recorded in any swallows recorded in a given patient. Interestingly, long-gap defects and occurrence of anastomotic leaks in the history of the patients—leading to surgical difficulties and more severe esophageal wall injuries—were predominantly encountered in this group. Similar to the pressurization pattern group, fundoplication procedures conducted in 8 of 15 patients may also have played a significant role in the disturbance of esophageal motility.

Esophageal motility patterns were not predictive of symptoms. Finding asymptomatic patients in all 3 esophageal motility patterns can be somewhat surprising; however, even if one could easily think that most symptomatic patients should be the ones with the least amount of peristalsis, a recent study has demonstrated that there is a lack of correlation between perception of dysphagia and esophageal manometry parameters (25). Moreover, because children with EA have never known what a “normal” peristalsis is, it may difficult or even impossible for them to characterize their way of eating as being “abnormal.” These children may have adapted well to their unique situation. On the contrary, patients from all 3 esophageal motility patterns demonstrated similar symptoms of dysphagia and modification of their alimentary habits. We also found that esophagitis was found in children belonging to the aperistalsis and pressurization groups; however, we are aware that these latter data may be prone to bias because all of the patients included in this study did not systematically undergo an esophagoscopy.

Indeed, one limitation of this study is its retrospective nature, which makes it prone to incomplete data collection precluding the possibility to correctly relate HREM results to endoscopy and pH findings; however, the principal aim of this study was not to correlate motility patterns to esophagitis or reflux index but rather to precisely describe the esophageal motor anomalies in this population and to correlate them with symptoms that were systematically assessed in all of the included patients.

Could HREM use in patients with EA help orient their management through childhood and adulthood? With the previous limitations, our findings are in keeping with those of Sistonen et al (6), who suggested that the underlying persistalsic abnormality could be responsible for an exacerbated stagnation of acid and pepsin in esophagus predisposing to more severe esophagitis and Barrett esophagus. Further prospective study is needed to confirm that upper GI endoscopy screening and follow-up with biopsies could be beneficial and, thus, should be intensified in patients with EA presenting a certain type of peristalsis motility pattern.

In conclusion, HREM helped characterize motility patterns in EA-repaired patients. Whether the use of HREM in EA-repaired patients with identification and classification of motility pattern may help orient choice of treatment and surveillance remains to be further determined.

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