

## Esophageal dysmotility: characterization and pathophysiology

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**SUMMARY.** Esophageal dysmotility is a considerable long-term issue in patients born with esophageal atresia (EA). To better characterize it, the normal esophageal motility is briefly reviewed with emphasis on the specific defects in EA. Multiple studies attempted to describe the dysmotility seen in patients with operated EA using esophageal manometry. Recently, high-resolution manometry has improved our understanding of normal esophageal motility. Using this new technology, it is now possible to better characterize the esophageal motility of patients operated on for EA. Three different patterns are described and presented: aperistalsis, pressurization, and distal peristalsis. Up to now, it has not been possible to find a correlation between the dysmotility severity and the patient's symptomatology. Different pathophysiological hypotheses of esophageal dysmotility in that population are discussed. Developmental neuronal defects are certainly present from the beginning. Surgical trauma can also contribute to the dysmotility. Finally, defective esophageal acid clearance capacity is a cause of gastroesophageal reflux disease, but the resultant esophagitis can also impair the normal esophageal function. The evolution of esophageal dysmotility in patients with repaired EA is not known and further studies will be necessary to clarify it.

**KEY WORDS:** dysmotility, esophageal atresia, esophageal manometry, trachea-esophageal fistula.

### INTRODUCTION

Esophageal dysmotility constitutes a considerable issue in esophageal atresia (EA) patients.<sup>1</sup> During the neonatal period, it can be a cause of prolonged initial hospitalization but will last a lifetime. It represents the most common problem in the long-term follow-up<sup>2</sup> and can evolve toward insidious long-term complications. In the clinical setting, esophageal motor dysfunction can be suspected because of the presence of different symptoms, but to characterize it, specific testing is needed. The goal of the presentation is to describe the types of esophageal dysmotility that present EA patients using high-resolution esophageal manometry (HREM). The hypothesized causes of this dysfunction will also be discussed.

Esophageal dysmotility manifests in the first weeks of life by clinical gastroesophageal reflux.<sup>3</sup> EA neonates will often present feeding difficulty and regurgitations. More severe cases will also present failure to thrive and respiratory symptoms. After

the introduction of solids, children will present an episode of food impaction. Anastomotic stenosis needs to be ruled out, but esophageal dysmotility combined with the fact that the active child will not take the time to chew enough are often the only etiologic factors identified. Later on, the older child and adolescent will learn how to avoid food impaction and will be described as 'slow eaters'. They will also be able to describe dysphagia, reflux, and heartburn. Gastroesophageal reflux is certainly related to anatomic factors of the gastroesophageal junction in this patient population, but esophageal dysmotility exacerbates the problem by decreasing the esophageal clearance. A significant proportion of EA patients are asymptomatic or simply not complaining of symptoms that have been present for their lifetime. Long-term follow-up is important because they can insidiously develop complications of chronic gastroesophageal reflux.

### CHARACTERIZATION OF ESOPHAGEAL DYSMOTILITY IN EA

Esophageal dysmotility can only be suspected on the symptoms basis, but further investigation is needed to characterize it. Esophagogram and endoscopy can

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show indirect signs of dysmotility such as dilation and retained food. Monitoring of the esophageal pH and multichannel intraluminal impedance can be used to identify and quantify the gastroesophageal reflux. Impedance has the advantage of providing a better assessment of the esophageal function by looking at the fluid movement inside of the esophagus. Fluid movement can also be evaluated by esophageal fluoroscopy and scintigraphy. However, esophageal manometry remains the gold standard to assess the esophageal motor function. Traditionally, it has been performed with water-perfused catheters that have a limited number of channels. Up to now, published data on long-term survivors of EA were obtained by standard manometry. Recently, HREM has revolutionized the study of esophageal motility. It uses solid-state catheters with multiple channels, providing more precise pressure topography plots<sup>4</sup> (Fig. 1).

The esophageal motility can be divided in three functional components: the upper esophageal sphincter (UES), the body, and the lower esophageal sphincter (LES). Few studies have looked at the esophageal motility in patients with EA. Most of them found a normal UES<sup>5-7</sup> except for Romeo *et al.*,<sup>8</sup> who studied newborns preoperatively and showed an incomplete relaxation in 10% of them. The LES is usually normal in EA patients, but reduced resting pressure and incomplete relaxation have been described in some.<sup>6,8-11</sup> The esophageal body is almost always affected in children with EA, and these anomalies persist in adulthood. Described anomalies include absence or uncoordinated peristaltic wave, simultaneous contraction, low amplitude contrac-

tion, and high baseline pressure.<sup>5-14</sup> Correlation with symptoms has been difficult to clarify. Abnormal motility has been found in asymptomatic patients.<sup>7</sup> One study found a correlation between the lack of distal esophageal contractions and the presence of gastroesophageal reflux disease.<sup>14</sup>

Using HREM, a multicenter study was conducted in patients with EA.<sup>15</sup> Thirty-five patients had type C EA, 5 had type A, and 6 had long gap. Automated measurements and visual analysis of the tracings were performed. A symptom questionnaire was filled out by the patient or parent. The tracings were analyzed according to the parameters published by Goldani *et al.* in 2010.<sup>16</sup> From the 40 patients, 6 had a long gap. Most of the patients had a primary repair ( $n = 35$ ), and fundoplication was performed in 18 patients. Seven patients were asymptomatic and had the HREM as part of the routine follow-up. Fifteen to thirty-two percent had gastroesophageal reflux symptoms such as heartburn, regurgitation, and vomiting; 34% had pulmonary symptoms (cough, recurrent pneumonia). Thirty-seven percent had dysphagia with solids. No patients exhibited a normal peristaltic pattern (Fig. 1). Three different patterns were identified: (1) complete aperistalsis (absence of contraction on all the swallows, Fig. 2); (2) pressurization (simultaneous contraction of the entire esophageal body following deglutition and with a normal LES relaxation, Fig. 3); (3) presence of middle or distal peristalsis (Fig. 4). Fifteen patients had aperistalsis (Fig. 2), 6 patients had pressurization (Fig. 3), and 19 patients had distal peristalsis (Fig. 4). All patients had a normal UES. Hypotonic LES was found in 16 patients, with 11 of them having aperi-

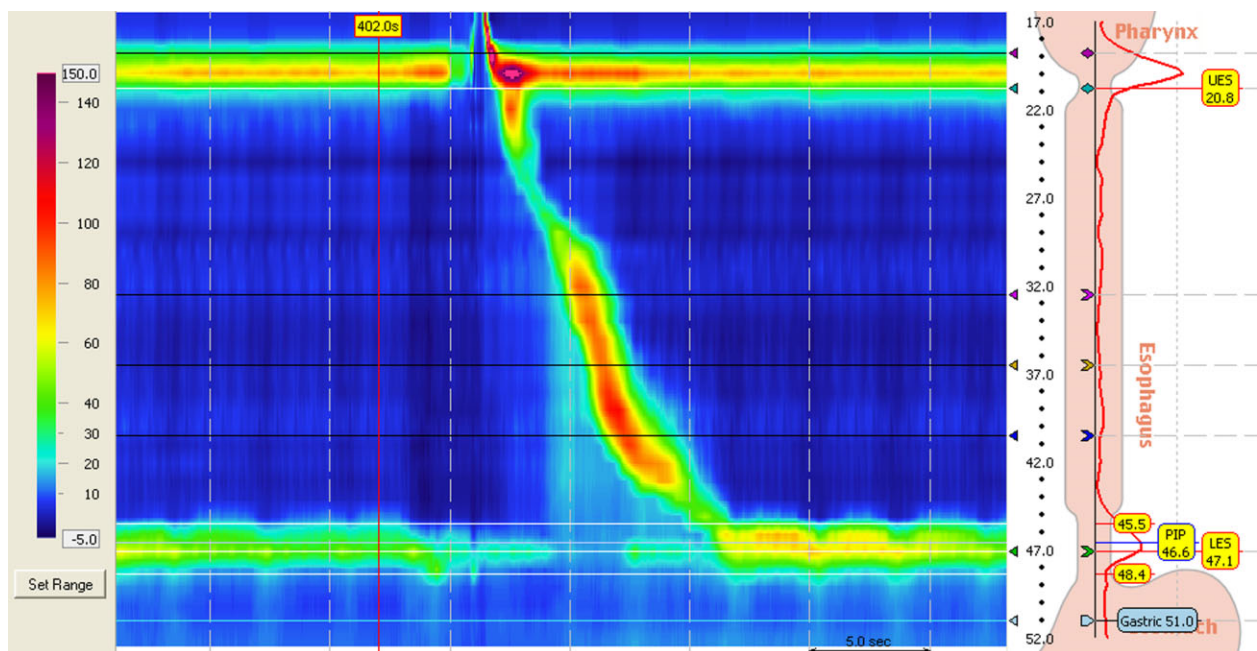


Fig. 1 Normal esophageal motility as assessed by high-resolution esophageal manometry.

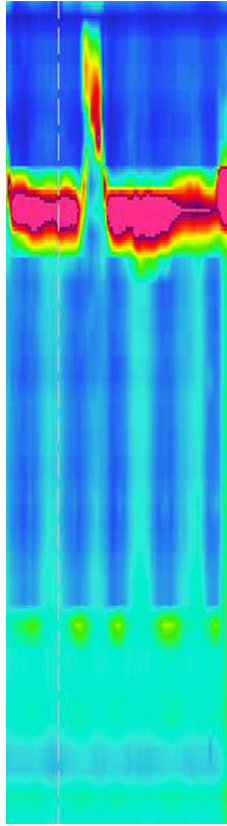


Fig. 2 Aperistalsis.

stalsis. Hypertonic LES was found in two patients (one with pressurization and one with distal peristalsis). It was possible to quantify the peristaltic activity only in the distal peristalsis group, but the amplitude of the contraction was below normal in all of them. There was no clear correlation between the symptoms and the motility patterns identified. Asymptomatic

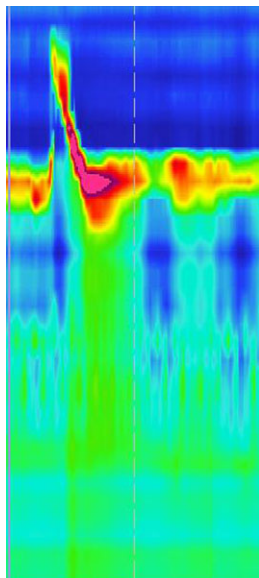


Fig. 3 Pressurization.

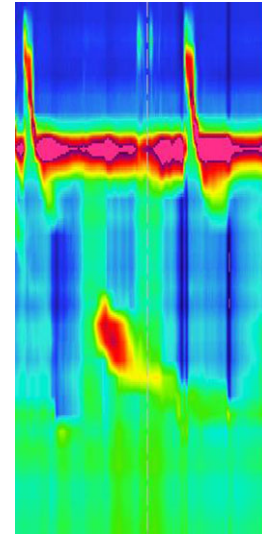


Fig. 4 Distal peristalsis.

patients were found in all the three patterns of dysmotility. However, there were statistically more patients with GER symptoms in the aperistalsis group than in the distal contraction group, which is concordant with a published study by Kawahara.<sup>14</sup> Interestingly, all the 19 patients who exhibited some distal peristalsis had a type C EA that was primarily repaired. These data confirm that the esophageal peristalsis is severely affected in all survivors of EA, but the type of dysmotility pattern is not clearly predictive of symptoms. Whether the use of HREM in EA might help orientate the choice of treatment and surveillance remains to be further determined.

#### PATHOPHYSIOLOGY OF ESOPHAGEAL DYSMOTILITY IN EA

The etiology of esophageal dysmotility found in long-term survivors of EA is still debated<sup>1</sup> but can be explained by three main hypotheses: developmental neuronal defects associated with the congenital anomaly, surgical traumatism, and esophagitis. There is increasing evidence from pathological analysis of developmental defects affecting both the esophagus<sup>17-20</sup> and the trachea.<sup>21</sup> Hypoganglionosis and immature ganglion cells in the myenteric plexus of the proximal esophageal atretic segment has been described.<sup>17</sup> In other studies, anomalies in the distal fistula were also found such as tracheobronchial remnants<sup>18</sup> and abnormal intrinsic innervation manifested by imbalance of neurotransmitters excretion and dysplasia of nerve plexus.<sup>19</sup> More recently, lower density and immaturity of interstitial cells of Cajal was demonstrated in the proximal and distal atretic esophagus.<sup>20</sup> Using an experimental rat model, Qi *et al.* demonstrated anomalies in the course and

branching pattern of the vagus nerves, deficient extrinsic nerve fiber plexus in the lower esophagus,<sup>22</sup> and intramural nervous abnormalities both excitatory and inhibitory.<sup>23</sup> Further evidence of primary dysmotility come from manometry studies performed preoperatively that demonstrated abnormal motility in newborn with EA<sup>8</sup> and in patients prior to isolated trachea-esophageal fistula.<sup>24–26</sup> Evidence of abnormal gastric motility has also been found in EA patients.<sup>27</sup>

Extensive mobilization and denervation of the esophagus during EA repair<sup>28</sup> is another mechanism that can affect the esophagus motor function. In a case report, a deterioration of esophageal motility after surgery was demonstrated by comparing the manometry pre- and postoperatively.<sup>29</sup> While unilateral vagotomy has no effect on peristalsis,<sup>30</sup> bilateral cervical vagotomy above the pharyngo-esophageal branches has been shown to abolish peristalsis in the striated muscle (proximal esophagus).<sup>31</sup> Fundoplication often becomes necessary in EA patients. This procedure is less likely to disrupt the esophageal innervation, but it can affect the clearance capacity of a dysfunctional esophageal body.<sup>32</sup> On the other hand, severe peptic esophagitis has been associated with peristaltic dysfunction both in adults<sup>33</sup> and in children.<sup>34</sup>

Esophageal dysmotility is present in all patients born with EA and has been demonstrated for all types and preoperatively. Surgical dissection and esophagitis can worsen the primarily affected esophageal motor function. Using HREM, it is now possible to better characterize it, but the clinical repercussion is still unpredictable. Long-term follow-up is thus essential for an optimal management of these patients.

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