Improved Assessment of Bolus Clearance in Patients With Achalasia Using High-Resolution Impedance Manometry

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Q4 Q5 **BACKGROUND & AIMS:** **Esophageal retention is typically evaluated by timed barium esophagram in patients treated for achalasia. Esophageal bolus clearance can also be evaluated using high-resolution impedance manometry. We evaluated the associations of conventional and novel high-resolution impedance manometry metrics, esophagram, and patient-reported outcomes (PROs) in achalasia.**

METHODS: **We performed a prospective study of 70 patients with achalasia (age, 20–81 y; 30 women) treated by pneumatic dilation or myotomy who underwent follow-up evaluations from April 2013 through December 2015 (median, 12 mo after treatment; range, 3–183 mo). Patients were assessed using timed-barium esophagrams, high-resolution impedance manometry, and PROs, determined from Eckardt scores (the primary outcome) and the brief esophageal dysphagia questionnaire. Barium column height was measured from esophagrams taken 5 minutes after ingestion of barium (200 mL). Impedance-manometry was analyzed for bolus transit (dichotomized) and with a customized MATLAB program (The MathWorks, Inc, Natick, MA) to calculate the esophageal impedance integral (EII) ratio.**

RESULTS: **Optimal cut points to identify a good PRO (defined as Eckardt score of ≤3) were esophagram barium column height of 3 cm (identified patients with a good PRO with 63% sensitivity and 75% specificity) and an EII ratio of 0.41 (identified patients with a good PRO with 83% sensitivity and 75% specificity). Complete bolus transit identified patients with a good PRO with 28% sensitivity and 75% specificity. Of the 25 patients who met these cut points for both esophagram barium column height and EII ratio, 23 (92%) had a good PRO. Of the 17 patients who met neither cut point, 14 (82%) had a poor PRO (Eckardt score above 3).**

CONCLUSIONS: **In a prospective study of 70 patients with achalasia, we found EII ratio identified patients with good PROs with higher levels of sensitivity (same specificity) than timed-barium esophagram or impedance-manometry bolus transit assessments. The EII ratio should be added to achalasia outcome evaluations that involve high-resolution impedance manometry as an independent measure and to complement timed-barium esophagram.**

Keywords: Outcome; Symptom; Esophagram; Swallow.

Q6 Q7 Achalasia is the prototypical esophageal motor disorder and is characterized by impaired deglutitive lower esophageal sphincter relaxation and absent peristalsis.[1,2] Bolus clearance is the fundamental function of the esophagus, which when disrupted by the motility abnormalities of achalasia results in esophageal retention and symptoms of esophageal dysphagia, chest pain, and regurgitation. Symptomatic improvement is an essential objective and often the primary outcome measure for gauging treatment response in achalasia. Nevertheless, discordance often is observed between patient symptoms and objective radiographic and manometric measures of esophageal function.[3–5] Esophageal retention, as measured by timed-barium esophagram (TBE), was shown to be more predictive of treatment failure in achalasia than symptom severity.[3] Therefore, in patients with previously treated achalasia, it is recommended that follow-up evaluations involve intermittent objective assessments, including TBE and/or manometry.[2]

Abbreviations used in this paper: **BEDQ, brief esophageal dysphagia questionnaire; BFT, bolus flow time; EGJ, esophagogastric junction; EII, esophageal impedance integral; HRIM, high-resolution impedance manometry; IQR, interquartile range; PRO, patient-reported outcome; TBE, timed barium esophagram.**

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Esophageal manometry is considered the primary method to assess esophageal motility and, when combined with multichannel intraluminal esophageal impedance sensors, the esophageal function evaluation can be enhanced by assessing the interplay between esophageal motility and bolus transit.[6,7] Use of esophageal impedance-manometry, however, was limited by its dichotomous qualitative evaluation of bolus clearance as complete or incomplete.[6,7] Advances in high-resolution impedance manometry (HRIM) offer an improved quantitative evaluation using a novel HRIM measure, the esophageal impedance integral (EII) ratio.[8] By using high-resolution impedance topography plots (Z-plots), the proportion of retained bolus can be quantified to better characterize esophageal bolus clearance.

We recently reported that the EII ratio outperformed other impedance-manometry metrics in correlating with symptoms among patients with dysphagia, but without a major esophageal motility disorder.[9] Given the benefits of assessing achalasia outcomes with TBE, we hypothesized that assessing achalasia patients during follow-up evaluation after treatment with the EII ratio would benefit the outcome evaluation. Thus, we aimed to evaluate the value of TBE, via barium column height, and HRIM, via the traditional dichotomized bolus transit, and the novel EII ratio, in assessing patient-reported outcome (PRO) in patients with achalasia after intervention.

Methods

Subjects

Patients with achalasia and previous treatment with pneumatic dilation, laparoscopic Heller's myotomy (often with Dor or Toupet fundoplasty), and/or per-oral endoscopic myotomy returning for follow-up evaluation or referred from elsewhere were prospectively recruited and evaluated. Seventy consecutive patients (without hiatal hernia $>$ 2 cm) evaluated between April 2013 and December 2015 who completed HRIM, symptom questionnaires, and TBE were included in the analysis; these patients have been described previously, although 5 patients from that report were excluded from this analysis because of technical issues with impedance sensors that prevented reliable analysis of HRIM measures of esophageal retention.[10] The time interval between evaluation and the most recent pneumatic dilation or myotomy was noted. When available, HRM performed before intervention was evaluated according to the Chicago Classification to provide an achalasia subtype.[1] When pretreatment manometry was not available, the diagnosis of achalasia was assumed based on reported manometry findings and subsequent treatment. The study protocol was approved by the Northwestern University Institutional Review Board.

Symptom Assessment

Symptoms were assessed by patient completion of written questionnaires at the time of HRIM. Questionnaires included the Eckardt score and the brief esophageal dysphagia questionnaire (BEDQ).[11] The Eckardt score (range, 0–12) was generated by the sum of scores for dysphagia, chest pain, and regurgitation based on the frequency of each symptom (0, never; 1, occasional; 2, daily; 3, with each meal) plus a score based on the degree of weight loss since the last therapeutic intervention (0, none; 1, $<$10 lbs; 2, 10–20 lbs; 3, $>$20 lbs). Patients reporting an Eckardt score $\leq$ 3 were considered a good PRO; those with Eckardt score $>$ 3 were considered a poor PRO.

The BEDQ is a validated questionnaire that consists of eight 6-point Likert scale questions (scored, 0–5) that assess the frequency and severity of dysphagia and odynophagia and 2 open-ended questions regarding frequency of food impactions and related emergency room visits.[12] Scores range from 0 (asymptomatic) to 50; a BEDQ score threshold of 10 was reported previously as an optimal score to diagnose major esophageal motor dysfunction and thus a BEDQ $<$ 10 was considered a good PRO; a BEDQ $\geq$ 10 was considered a poor PRO.

Timed Barium Esophagram Protocol and Analysis

Timed barium esophagrams were performed in the upright position with radiograph images of the esophagus obtained at 1, 2, and 5 minutes after ingestion of 200 mL of low-density (45% weight-to-volume) barium sulfate. The height of the barium column (in centimeters) at 5 minutes was measured vertically from the esophagogastric junction (EGJ).

High-Resolution Impedance Manometry Protocol and Analysis

After a minimum 6-hour fast, HRIM studies were completed using a 4.2-mm outer-diameter, solid-state assembly with 36 circumferential pressure sensors at 1-cm intervals and 18 impedance segments at 2-cm intervals placed transnasal to span from the hypopharynx to stomach (Medtronic, Inc, Shoreview, MN). After a 2-minute baseline recording, the HRIM protocol using a 0.45% saline solution included 10 swallows (5 mL) in a supine position and 5 swallows (5 mL) in the upright position.

Manometry studies were analyzed using ManoView version 3.0 analysis software (Medtronic, Inc) according to the Chicago Classification.[1,13] Esophageal motility diagnoses were designated from the supine swallows in accordance with the Chicago Classification v3.0, using a median integrated relaxation pressure of more than 15 mm Hg as the upper limit of normal.[1] Although the Chicago Classification was designed and intended for patients without previous