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Conflict of interest
The authors disclose the following: Prateek Sharma serves as a consultant for Takeda Pharmaceuticals. Philip Katz serves as a consultant for Torax.

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Esophageal Mucosal Impedance: Is It Time to Forgo Prolonged Gastroesophageal Reflux Recordings?

See "Mucosal impedance discriminates GERD from non-GERD conditions," by Ates F, Yuksel ES, Higginbotham T, et al, on page 334.

For several decades, ambulatory 24-hour esophageal pH monitoring remained the sole tool for the assessment of gastroesophageal reflux. This tool, first introduced in 1969, is still being used to determine the extent of esophageal acid exposure in patients with gastroesophageal reflux disease (GERD) with typical or atypical symptoms, patients who are candidates for surgical fundoplication and those who do respond to antireflux treatment.[1,2] However, it has been repeatedly demonstrated that the catheter-based pH testing interferes with patients' reflux-provoking activities (food consumption, smoking, sleep, etc) primarily owing to a variety of side effects, including nose pain, runny nose, throat pain, throat discomfort, cough, chest discomfort, and headache.[3,4] Consequently, not uncommonly GERD patients with significant esophageal mucosal involvement (erosive esophagitis, Barrett's esophagus, and others) or significant predisposing factors for gastroesophageal reflux demonstrated a normal pH test. Importantly, this was the main impetus for the development of the wireless pH capsule, which represented an attempt to improve patients' tolerability and thus the accuracy of the pH test both by reducing the impact of the test on patients' normal daily activities and by increasing its duration.[5,6] In addition, the wireless pH capsule offered a new direction in technological development, which is miniaturization of esophageal function testing.[7] However, the impedance + pH test, which was introduced in 1991 but approved by the Food and Drug Administration only in 2002, brought back the catheter-based assessment of gastroesophageal reflux.[8] The main advantage of the impedance + pH test over the catheter-based pH test is the ability to determine the presence of gastroesophageal reflux through impedance rather than pH changes.[9] Thus, impedance + pH can identify a reflux event through series of changes in esophageal impedance that occur sequentially from the distal to the proximal part of the esophagus. The pH sensor, which is embedded within 5 cm from the tip of the probe, determines if the reflux is acidic ($pH < 4$), weakly acidic ($4 \leq pH < 7$), neutral ($pH = 7$), or alkaline ($pH > 7$). Furthermore, the impedance changes can demonstrate if the reflux is liquid or mixed (gas + liquid), characteristics that seem to be important for esophageal sensation and thus symptom generation.[10]

In this issue of *Gastroenterology*, Ates et al[11] have reported on a novel technique, named mucosal impedance, that can discriminate between GERD and non-GERD conditions. The authors developed and validated a catheter that can traverse through the working channel of a regular endoscope and can measure the impedance of the esophageal mucosa through direct mucosal contact.[12] Two circumferential sensing rings, 3 mm in length and 2 mm apart, are mounted on a catheter with the distal ring 1 mm away from the tip. By applying a slight mucosal pressure, electrical conductivity between the 2 rings could be measured and, consequently, the impedance of the mucosa could be determined. Because there is an inverse relationship between electrical conductivity and impedance, an increase in electrical conductivity results in decrease in impedance and vice versa. In their study, the authors compared mucosal impedance values of 5 different groups of patients, erosive esophagitis, nonerosive reflux disease, functional heartburn, eosinophilic esophagitis, and achalasia. Mucosal impedance measurements were obtained at 2, 5, and 10 cm above the gastroesophageal junction. The authors were able to demonstrate that patients with GERD had lower mucosal impedance values compared with non-GERD patients. In addition, patients with eosinophilic esophagitis had the lowest mucosal impedance values, which remain the same throughout the esophagus, unlike the others, which demonstrated an increase in mucosal impedance between distal and proximal esophageal measurements.

Although the study demonstrated that mucosal impedance assessment can differentiate GERD patients from those who do not have GERD, the main question is what factors determine mucosal impedance? This is a pivotal question, because these factors will drive the results of the test. The impedance + pH test measures the impedance of esophageal content that passes between 2 sensing rings and thus determines the characteristics of the content (gas, liquid, or both) and if the content moves orad or caudad. The surrounding esophageal tissue provides the baseline impedance measurements, ranging from 1500 to 4000 Ohm, when the impedance + pH catheter is placed in the esophageal lumen. Erosive esophagitis and Barrett's esophagus have been shown to reduce baseline impedance levels.[13] However, the mucosal impedance catheter measures transepithelial resistance and permeability, which are driven by mucosal structural changes.[14] Consequently, any injurious agent that compromises epithelial integrity may lead to mucosal structural changes that can result in alteration of mucosal impedance recordings. Although injurious agents related to gastroesophageal reflux are very common, other, non–reflux-related injurious agents (eg, medications, fungal and viral infections) can also result in structural abnormalities that are likely to be associated with impedance changes. The non–reflux-related esophageal mucosal structure abnormalities may not be differentiated from reflux-related esophageal mucosal changes by the mucosal impedance catheter. Interestingly, in this study patients with achalasia demonstrated a higher mucosal impedance values even when compared with functional heartburn patients. Patients with long-standing achalasia tend to develop friability of the esophageal lining owing to luminal stasis which denotes chronic mucosal inflammation.[15,16]

A more important question is whether mucosal impedance testing will replace gastroesophageal reflux testing (impedance + pH, catheter-based pH testing, and the wireless pH capsule). Although mucosal impedance testing is simple and easy to perform, it provides no information on the degree, type, and patterns of a patient's gastroesophageal reflux. Mucosal impedance testing is unable to differentiate between acidic and nonacidic mucosal structural changes, which require different therapeutic approaches.[17,18] In addition, it does not have the capability of determining whether a patient's reflux is primarily during nighttime or daytime. Again, each reflux pattern may require a different therapeutic strategy.[19,20] Mucosal impedance is also unable to determine the height of reflux episodes and the association between reflux events and symptoms. The technique also has limited value in assessing improvement, although not necessarily normalization, of gastroesophageal reflux after medical, endoscopic, or