Pleotropic Effects of Proton Pump Inhibitors
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Comparison of Investigation Modalities for Evaluation of Esophageal Peristaltic Function

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Summary **We reviewed the recent literature concerning investigations of esophageal peristaltic function. The gold standard for the assessment of esophageal peristaltic function is manometry with pH monitoring. Even with this investigation modality, however, we are in fact doing no more than estimating esophageal peristaltic function from the manometry and pH results. With esophageal fluoroscopy and scintigraphy, where we observe esophageal motility, there are problems with radiation exposure and handling of radioactive agents that make widespread use difficult. In recent years, the development of multichannel intraluminal impedance (MII) manometry has allowed simultaneous measurement of intraesophageal pressure and assessment of esophageal peristalsis. Using MII it is also possible to distinguish whether gas or liquid is passing down the esophagus. When manometry is performed in conjunction with transnasal esophagogastroduodenoscopy, with this unique combination it is possible to measure the intraesophageal pressure while actually observing the swallowing motion at the same time. Assessment of esophageal peristaltic function is now moving from simple measurement of intraesophageal pressure to simultaneous impedance manometry and endoscopic observation of esophageal peristalsis itself.**

Key Words: **esophageal peristalsis, manometry, transnasal esophagogastroduodenoscopy**

Introduction

The main function of the esophagus is to transport food boluses from the pharynx to the stomach through peristaltic motion. This occurs through the primary peristaltic wave, triggered by swallowing, passing from the upper to lower esophagus in a sequence of rostral contractions and caudal relaxations. There are also secondary peristaltic waves that are triggered by intraesophageal dilatory stimuli. Investigation modalities for evaluation of esophageal peristaltic function include esophageal manometry [*1*], esophageal radiography (barium swallow) [*2*], esophageal scintigraphy [*3*], ultrasonography [*4*], and impedance methods [*5*]. Of these, esophageal manometry allows quantitative assessment of esophageal motility as well as simultaneous pH monitoring, making it the gold standard investigation modality for evaluation of esophageal peristaltic function.

Esophageal Manometry

Esophageal manometry methods use either an infusion catheter or microtransducer. In the infusion catheter method, a very small flow of distilled water passes through a side

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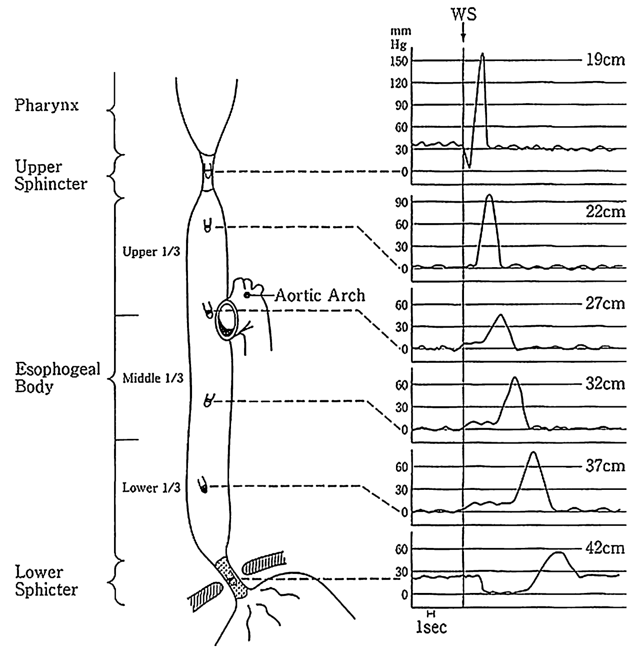

Fig. 1. Manometric readings at each position during a wet swallow (WS). Reprinted with permission [*6*].

hole in the catheter sensor, and motion of the gastrointestinal tract that blocks this flow is measured as the intralumenal pressure. The merits of this system are that the catheter sensors are inexpensive, and successive measurements can be readily performed. Its main demerit is that the equipment is massive, and although suitable for bedside use is not easily carried, making prolonged recordings difficult. The microtransducer method senses changes in intralumenal pressure as distortions of the direct pressure sensor, and transforms them into electrical signals. A pump is not needed to circulate water, as with the infusion catheter method, so only a portable recorder is needed. This makes prolonged recordings possible. The main demerit of this method is that the sensors are expensive and fragile. In Figure 1, we show the primary peristaltic wave accompanying swallowing as recorded using the infusion catheter method by Dodds *et al.* [*6*]. The rostral 1/3 of the muscular esophagus is skeletal muscle, so in this section the peristaltic wave is high in amplitude, the contraction time short, and transmission rapid. The transition zone between skeletal and smooth muscle is located at the level of the aortic arch, and here the peristaltic wave is lowest in amplitude and transmission slowest. The caudal 2/3 of the muscular esophagus is smooth muscle, and as the peristaltic wave approaches the lower esophageal sphincter (LES), its amplitude increases and the contraction time becomes longer.

Esophageal peristaltic waves are of twp types: the primary peristaltic wave that accompanies swallowing, and secondary peristaltic waves that arise in the esophagus itself, independent of swallowing. Secondary peristaltic waves are considered to serve the function of transporting food boluses left in the esophagus, and clear refluxed material. Kusano *et al.* [*7*] induced secondary peristaltic waves using a slow liquid infusion of 0.1 N saline, and suppressed this reaction with atropine sulphate.

Esophageal Fluoroscopy

Esophageal fluoroscopy using barium can be performed at any medical institution. Common findings of esophageal dysmotility are stasis or reflux of barium, and 'corkscrew esophagus'. The shortcomings of fluoroscopy are its inability to quantify, and radiation exposure to the patient. Reports are therefore common of conditions such as achalasia where barium is retained within the esophagus for prolonged periods. Montazeri *et al.* [*8*, *9*] suggest that the surface area of barium retention is useful in diagnosing the severity of disease, and for assessing LES pressure following balloon dilatation.

Kahlaris *et al.* performed esophageal fluoroscopy using barium simultaneously with esophageal manometry, recording changes with time in both fluoroscopic images and the manometry trace (Fig. 2). The tracings from the video images on the right show the distribution of the barium column at the times indicated above the individual tracings and by arrows on the manometric record. Example at 4.2 s, the peristaltic contraction was beginning at the third recording site and correspondingly, the tail of the barium bolus was located at the third recording site. At 13.8 s, after completion of the peristaltic contraction, all of the barium had been cleared into the stomach [*10*].

Esophageal Scintigraphy

Although nuclear medicine studies of gastrointestinal motility are considered by some to be the gold standard, few institutions actually perform these investigations. Scintigraphy is a safe method that causes little discomfort to patients, allows quantitative physiological evaluation of swallowing, and is suitable for objective screening of esophageal dysmotility [*11*]. Despite these advantages, in Japan esophageal scintigraphy is not covered by medical insurance, the radioactive test materials are expensive, and its application is strictly regulated, requiring the approval of the hospital ethics committee. Nakajima *et al.* [*12*] performed esophageal scintigraphy on 35 patients with systemic sclerosis (scleroderma), finding localized abnormalities in 13%, and diffuse abnormalities in 50% of patients.

In recent years, magnetic resonance imaging (MRI) has been used to assess esophageal function [*13*], and further advances can be anticipated with this investigation modality.

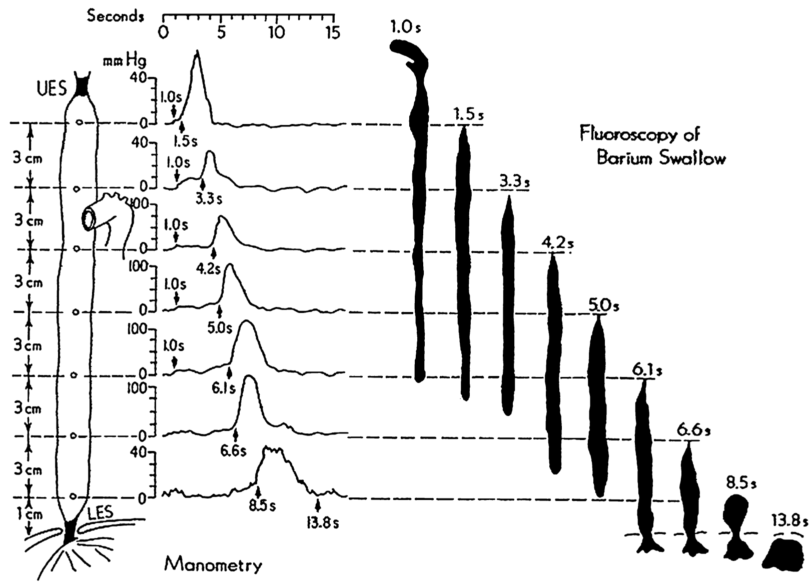

Fig. 2. Simultaneous manometry and fluoroscopy of a barium swallow. Reprinted with permission [*10*].

Table 1. The effects of lansoprazole and famotidine on esophageal wall thickness in GERD patients. Reprinted with permission [*18*].

	Pretreatment	After 6 week	After 12 week
Group 1			
Total wall thickness	4.28 ± 0.3*	2.7 ± 0.34†	3.34 ± 0.94*‡
Submucosal layer	1.65 ± 0.4*	1.16 ± 0.19†	1.44 ± 0.34
Muscularis propria layer	1.46 ± 0.41	1.05 ± 0.17	1.20 ± 0.24
Group 2			
Total wall thickness	4.06 ± 0.3*	4.48 ± 1.11*†	2.92 ± 0.73‡
Submucosal layer	1.46 ± 0.48	1.75 ± 0.48	1.28 ± 0.3‡
Muscularis propria layer	1.24 ± 0.25	1.55 ± 0.47	1.1 ± 0.2

*p<0.005 vs control; †p<0.01 vs pretreatment; ‡p<0.01 vs after 6 weeks treatment.

Ultrasonography

Using an ultrathin ultrasound probe, we can observe the thickness and movement of the esophageal longitudinal and circular muscle. Yamamoto *et al.* [*4*] found that the thickness of both longitudinal and circular muscle increases during peristalsis. Holloway *et al.* [*14*] reported that esophageal muscle thickness correlates with the degree of impairment of swallowing. Kawamura *et al.* [*15*] found hypertrophy and structural abnormalities of the esophageal wall in patients with advanced esophagitis, and that inflammation extending to the muscular layer impairs LES function. Furthermore, Mittal *et al.* [*16*] reported that the muscle thickness of the esophageal body is important in assessing esophageal function in patients with primary esophageal motility disorders such as achalasia. Interestingly, studies performed in recent years with simultaneous manometry and ultrasonography have shown increased muscle thickness in patients with esophageal symptoms but normal intresophageal pressures [*17*].

Mine *et al.* [*18*] reported hypertrophy of the lower esophageal wall, in particular the submucosal layer, in gastroesophageal reflux (GERD) patients in comparison with healthy volunteers. This hypertrophy improved with 6 weeks of lansoprazole therapy, but not with famotidine (Table 3).

Impedance Method

The multichannel intraluminal impedance (MII) method has attracted much attention in recent years. It can distinguish between esophageal boluses of gastric juice, food and air by their electrical resistance. Using a multichannel

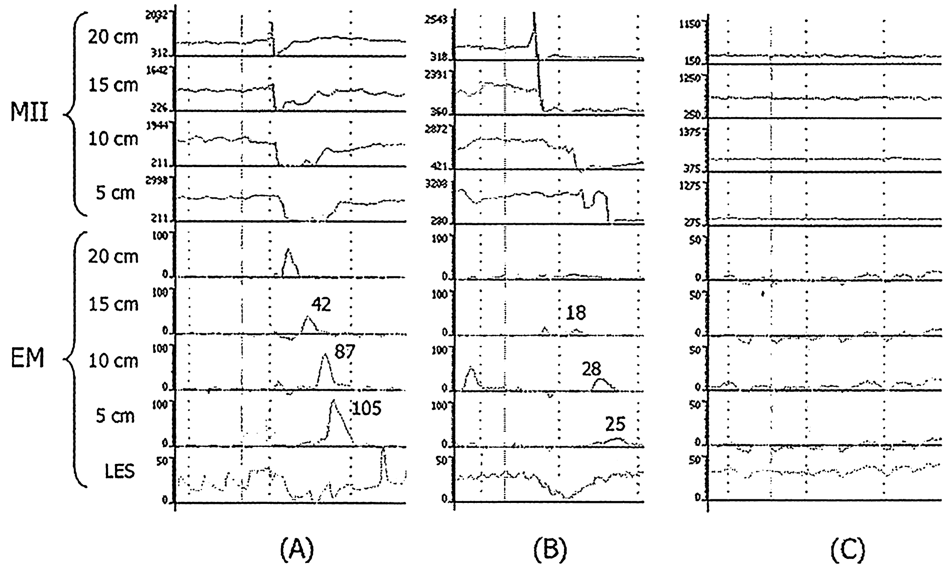

Fig. 3. Simultaneous multichannel intraluminal impedance (MII) and esoghageal manometry (EM). A: Manometry of normal peristaltic complete bolus transit; B: Manometry of ineffective contraction with incomplete bolus transit; C: Aperistalsis with incomplete bolus transit (typically seen in achalasia). Reprinted with permission [*20*].

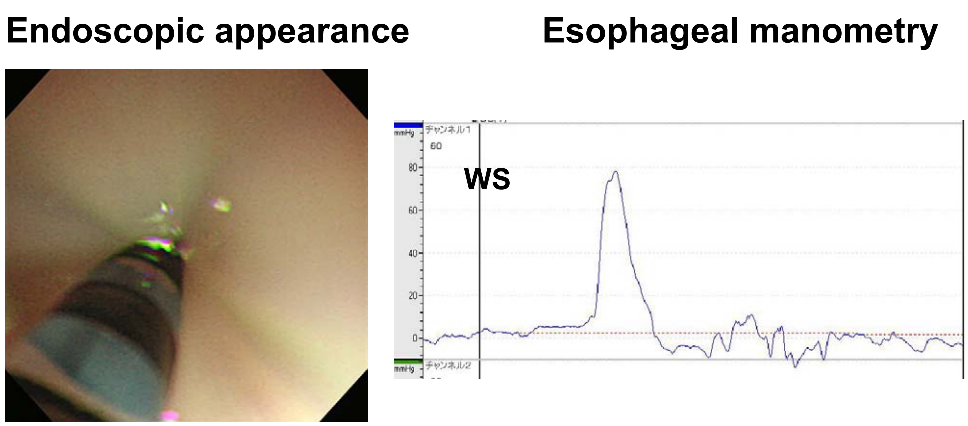

Fig. 4. Simultaneous transnasal esophagoscopy and esophageal manometry, after Kawai *et al.* [*21*]. In this healthy volunteer, we can see the endoscopic appearance of a peristaltic contraction (left) and a peak intraesophageal pressure of 80 mmHg (right).

catheter, a bolus can be followed down the esophagus, and reflux assessed, without radiation exposure to the patient. Using the combination of MII with esophageal manometry (MII-EM), the intraesophageal pressure in the lower esophagus required to clear a liquid bolus from the esophagus was shown to be 30 mmHg [*19*]. This agrees with the results of Kahrilas *et al.* [*10*], who performed simultaneous barium fluoroscopy and intraesophageal manometry, and reported that barium was retained in the esophagus if the amplitude of the primary peristaltic wave in the lower esophagus fell below 25 mmHg, and indicates that MMI-EM is a superior investigation modality that provides simultaneous information regarding esophageal peristalsis and intraesophageal pressure. Tutuian *et al.* performed MMI-EM in 350 patients, with representative results shown in Fig. 3 [*20*].

Novel Tests of Esophageal Function

Until now, manometry has involved the introduction of an intraesophageal manometry probe only into the esophagus, so the pressure waveform has been used to estimate peristalsis. Transnasal esophagogastroduodenoscopy (TN-EGD) uses an ultrathin endoscope with an outside diameter of only 4–5 mm, and as it is introduced into the esophagus without contacting the base of the tongue, swallowing is possible during the procedure. Kawai *et al.* [*21*] attempted to assess esophageal peristalsis using TN-EGD. In other words, they

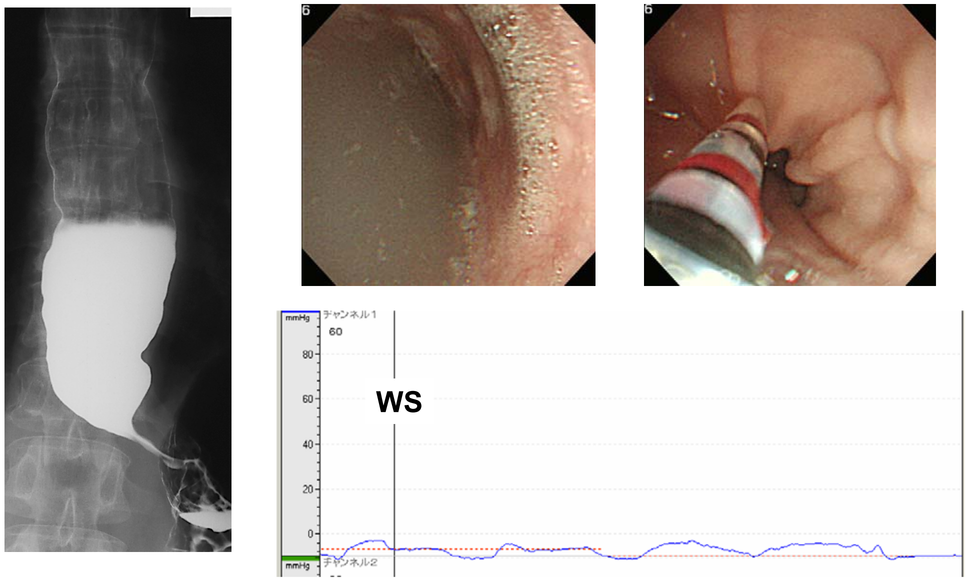

Fig. 5. Simultaneous transnasal esophagoscopy and esophageal manometry, after Kawai *et al.* [*21*]. In this patient with achalasia, we can see the fluoroscopic appearance of a barium swallow (left), the appearance as the endoscope is introduced into the esophagus (residual fluid is present) (upper middle), no evidence of a peristaltic contraction at the time of manometry (upper right), and only minor movement around the baseline on manometry (lower).

observed peristalsis in healthy volunteers using a transnasal endoscope, and introduced a 5 Fr manometry catheter through the instrument channel for simultaneous real-time measurements of intraesophageal pressure. They observed the peristaltic contraction in the lower esophagus endoscopically, and recorded the intraesophageal pressure at the same time (Fig. 4). In a patient with achalasia, there is no sign of a normal peristaltic contraction endoscopically, no evidence of a peristaltic wave, and only some wavering around the baseline on manometry (Fig. 5). This combination of simultaneous endoscopy and manometry shows promise for the screening of peristaltic function.

Conclusion

Esophageal dysmotility conditions can be broadly divided into primary esophageal motility disorders such as achalasia, and secondary esophageal motility disorders, such as is seen in patients with GERD. Although disorders of esophageal peristalsis are not a major factor in patients with mild GERD of Savary-Miller grade I or II, reduced peristaltic contraction pressure in the lower esophagus has been reported in patients with grade III and IV disease[*22*, *23*]. The prevalence of *Helicobacter pylori* infection is expected to decline further in Japan, and as a consequence the number of GERD patients will undoubtedly increase. We are also seeing more patients with endoscopy negative GERD (NERD) and functional heartburn, so assessment of esophageal peristaltic function will become increasingly important in the diagnosis of a variety of esophageal disorders.

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