EndoFLIP Topography: Motor Patterns in an Obstructed Esophagus

Esophageal distension–induced secondary peristalsis plays an important role in the clearance of gastric contents refluxed into the esophagus and in the expulsion of food residues left behind by swallow-induced primary peristalsis. Esophageal motor responses to distension have been investigated using water-filled balloons monitoring esophageal pressures proximal and distal to the balloon. Recently, motor patterns using a fluid-filled obstructing balloon with or without recording pressures proximal or distal to the balloon have measured impedance that may provide information on the luminal cross-sectional area (CSA).[1]

Functional lumen imaging probe (FLIP) records luminal CSAs per diameter using 17 ring electrodes spaced 1 cm apart to provide impedance data from 16 sites in a long balloon filled with fluid.[2] FLIP planimetry reporting some "unique" motor patterns such as distension-induced repetitive contractions in health and disease[3,4] has been proposed as an alternative to high-resolution manometry topography. However, the pathophysiologic basis of findings and their relationship to previously described motor patterns remains unknown.

The esophagus is wired to elicit either centrally organized swallow-associated primary peristalsis, locally regulated secondary esophageal peristalsis, or related abnormalities. It may also exhibit spontaneous, disorganized contractions termed tertiary contractions. Esophageal distension may augment these contractions. It is not clear whether the motor patterns recorded by endoluminal FLIP (EndoFLIP) are extensions of known pathophysiologic or any novel patterns.

Primary Peristalsis

The swallowing reflex produces primary peristalsis that can be elicited by the stimulation of either the superior laryngeal nerve (SLN) or recurrent laryngeal nerve. Although a solitary simulation of the SLN causes a single primary peristaltic sequence, sustained afferent nerve stimulation may cause repeated swallows.[5,6] One circuit involves the nucleus ambiguous that by activating lower motor neurons elicits primary peristalsis in the striated muscle of the oral cavity, pharynx, upper esophageal sphincter, and cervical esophagus. This sequence of events results in the delivery of a food bolus into the cervical esophagus.[7]

The other circuit involves inhibitory and excitatory parasympathetic preganglionic neurons in the dorsal motor nucleus of the vagus. Swallowing causes prompt activation of intramural inhibitory and sequential activation of the excitatory neurons responsible for the peristalsis in the esophageal smooth muscle.[8] The inhibitory circuit is responsible for the so-called deglutitive inhibition and thus for the latency of onset of contraction and the rebound contraction.[9,10] The excitatory circuit influences latency and contributes to the contraction.[11] The peristaltic response in the smooth muscle part of the esophagus resembles that of vagal efferent stimulation except that the swallow-induced peristalsis has a slower speed of propagation.[8] Swallow-induced esophageal peristalsis is generally similar in awake or anesthetized subjects.[12] In some cases, however, the peristaltic wave may show a delay at the junction of the upper one-third vs the lower two-thirds of the esophagus.

Multiple repetitive 2-mL swallows at shorter intervals (as during rapid drinking of water) suppresses contractile responses to all swallows except for the last one. In healthy subjects, an interval of about 8 seconds was found to be optimal for the complete peristaltic sequence. Behar and Biancani[13] reported that paired swallows 5 seconds apart in control subjects with a normal rate of peristalsis (with the latency of contraction at the distal-most part of the esophagus of 6.4 seconds) elicited only 1 contraction at the end of the second swallow. However, rapid peristalsis (with a latency of 2.9 seconds), presumably because of loss of inhibitory neuromuscular transmission, elicited 2 contractions, 2 each to 2 swallows. Behar and Biancani[13] suggested that the interswallow interval is critical in documenting impaired inhibitory neurotransmission. Differences in the duration of latency of contraction at different esophageal sites may explain the shorter interval for the full contractions in the proximal vs distal part.

Fornari et al[14] observed that the last contraction after repetitive swallows is usually larger than that with single swallows. The mechanism of the large contraction (also known as reserve contraction) is not known. Swallowing-induced activation of the longitudinal muscle may support peristaltic contraction mediated by the circular muscle. In addition, contraction of the longitudinal muscle by an overall shortening of the esophagus may cause retrograde displacement of the lower esophageal sphincter (LES).[15,16]

Secondary Peristalsis

In the smooth muscle part of the esophagus, transient balloon distension elicits secondary peristalsis that is characterized by isolated esophageal peristalsis without a pharyngeal or cricopharyngeal response,[12] with variable responses in the upper esophageal sphincter.[17] Esophageal pressure recording at sites proximal and distal to the balloon shows that secondary peristaltic contractions involve both striated and smooth muscle portions of the esophagus. Additionally, the junctional area between the proximal and distal esophagus shows a delay in the progress of the peristaltic contraction that is exaggerated by atropine

(in experimental animals and humans) in response to swallowing.[18] Simultaneous recordings of intraluminal pressures and membrane potentials revealed that hyperpolarization (indicating muscle inhibition) is responsible for the latency of contraction or depolarization.[19]

Repeated successive transient balloon distension caused an inhibition during the period of stimulation followed by a prominent contraction to the last distension.[18] This response is similar to that of primary peristalsis in humans. In some cases, however, a peristaltic response to the first stimulus in the series was observed. These studies are consistent with the view that the motor part of esophageal peristalsis uses the same neural circuits for primary or secondary peristalsis. However, the contribution of the cholinergic component in the 2 contractions may differ.[20]

Esophageal Propulsive Force

Sustained esophageal distension elicits contraction proximally and inhibition distally, dissecting the excitatory and inhibitory components of the peristalsis. This sequence of events facilitates the movement of the bolus retained in the esophagus. Winship and Zboralske[21] reported that in the human esophagus longer distensions using large volumes evoked aboral force to propel the obstructing balloon into the stomach. The propulsive force occurred promptly and was sustained until the balloon was deflation. Conversely, the detachment of the obstructing balloon converted the stationary propulsive force to a propagating type, leading to the forward propulsion of the balloon at a speed of 4 to 8 cm/s. Arresting the balloon movement also arrested the propagating force and converted it into a stationary propulsive force until the balloon was freed when the propagating force delivered the balloon to the stomach. Esophageal obstruction promotes a collection of secretions proximal to the obstruction inducing swallowing, which initially inhibits but later at the time of contraction wave augments the propulsive force.[21]

Paterson and colleagues[18] recorded esophageal pressures distal to a distended balloon, mimicking transient obstruction. Distal to the balloon, esophageal motor activity was inhibited at the onset and for the duration of the balloon distension. The inhibition extended to the LES. The pressure sensor was pinned to the sphincter to ensure that the LES relaxation was not a movement artifact. Simultaneous membrane potential recording using suction electrodes showed that early and late inhibition during maintained distension were associated with smooth muscle membrane hyperpolarization.[19]

Deflation of the balloon led to the peristaltic contractile activity distal to the balloon and LES relaxation followed by its contraction. These observations agree with the initial reports that in vitro sustained distension elicits contractions on termination of esophageal circular smooth muscle distension.[18] These observations correlate with those of esophageal propulsive force.[21] Esophageal obstruction elicits secondary peristalsis proximally up to the point of obstruction, which is converted into stationary esophageal propulsive force once the obstruction is removed, denoted by the peristaltic contraction. The distal inhibition was dependent on the degree of distension. However, the secondary peristaltic wave continued over the balloon onto the esophagus beyond the balloon. The authors noted that almost one-third of the secondary peristaltic contractions may be expressed in the distended balloon extending to the distal esophagus.

Contractions on an Obstructed Balloon

Rao et al[22] investigated the effect of intraesophageal balloon distension on esophageal contractions over, proximal, and distal to the balloon. A 4-fold increase in the CSA of the balloon was associated with a 20-fold increase in the motility index over the balloon related to the frequency, amplitude, and duration of contractions. The motor activity increased proximal to the balloon but not so much distally. The authors recognized 3 types of contractions: swallow-induced primary and distension-induced secondary peristaltic contractions, and distension-induced and spontaneous, nonperistaltic tertiary contractions.[22] The distension-induced and spontaneous tertiary contractions are confined to the balloon and are also called localized, nonpropagating pressure waves. Primary and secondary peristaltic contractions start and are arrested proximal to the balloon and contribute to the esophageal propulsive force. However, they may continue over the balloon and beyond it to the distal esophagus.[18] Esophageal distension-induced secondary peristaltic contraction is associated with distal inhibition, and it is usually expressed distally only after balloon deflation. When secondary peristaltic contraction continues over and beyond a distended balloon, its amplitude is reduced consistent with persistent distal inhibition.[18,23] Sustained esophageal distension has an inhibitory effect on primary as well as secondary peristalsis distal to the balloon.

Sustained balloon distension is associated with esophageal obstruction and difficulty in handling salivary secretion.[21,23] Pharyngeal collection of secretion may elicit swallow-induced primary peristalsis by stimulating the SLN and recurrent laryngeal nerve.[6] Because the expression of the peristaltic waves depends on the interswallow interval, only swallows with a sufficient interval may be fully expressed, whereas others are suppressed. Swallow-induced primary peristalsis may be arrested proximal to the balloon and augment the esophageal propulsive force. However, many primary peristaltic waves may be expressed over and beyond the distended balloon. Interestingly, a 9-second stimulation of the SLN is reported to elicit 2 full primary peristaltic contractions.[5]

Contractile Responses Using Impedance Planimetry

Barium swallow and barium videography have been used for the estimation of esophageal diameter and

progress of intraluminal contents. Impedance planimetry, on the other hand, has been introduced as a nonradiologic technique to study the luminal diameter and contractile patterns during the movements of luminal contents.[1] It may also provide data on the mechanical properties of the muscular wall. This technique identified 2 types of motor activities in the intestine: lumen-occluding motor patterns and myogenic rhythmic myogenic contractions. Lumen-occluding motor patterns with large changes in the CSAs were associated with the movement of intraluminal contents. These neural reflexes were blocked by a ganglionic blocker, hexamethonium. Different parts of the gut revealed distinct neurogenic motor patterns. The second, type, myogenic rhythmic myogenic contractions (resistant to hexamethonium), was associated with the pendular movements involved in the mixing of luminal contents. Such myogenic contractions may be coupled with interstitial cells of Cajal when present.[24]

Orvar et al[23] found that inflation of the balloon causes volume-dependent transient decreases in the CSA that correlate with an increase in intraballoon pressure. The contraction waves augmented on increasing pressures were called reactive contractions. The reactivity was prominent in subjects with chest pain.[22,23] The authors[22,23] also carefully monitored swallow and esophageal contractions proximal to the balloon and noted that many contractions over the balloon were associated with swallows or secondary peristalsis.

Using EndoFLIP planimetry Carlson et al[2] recorded changes in the CSA from 16 points, 1 cm apart covering the distal esophagus, LES, and stomach. The transient changes in the CSA represented the intraluminal pressure. They recorded a spectrum of distension-associated esophageal contractions. In healthy subjects, distension elicited anterograde waves, which appeared to start at the proximal end of the balloon, progressing distally. The anterograde progression was due to a progressive increase in the latency of contraction distally along the esophagus. These waves were associated with the LES opening and migrating proximally with the onset of the contraction wave and finally closing on the arrival of the contraction wave. Such waves could represent primary or secondary peristaltic contractions over the balloon.[22] These waves occurred singly or in groups. When this cluster of waves fulfilled certain criteria such as the so-called rule of 6, they were named anterograde rhythmic contractions (ARCs).[3] The high-resolution motility study showed normal primary peristalsis missed ARCs in most subjects (8/10).

The presence of ARCs was correlated with repeated swallows greater than 8 seconds apart, and EndoFLIP planimetry was proposed to avoid a separate high-resolution manometry topography study. Swallow-induced primary peristalsis on an obstructed balloon has been attributed to difficulty in handling secretions triggering the swallowing reflex.[21,22] Interestingly, persistent stimulation of the SLN may elicit repeated swallowing at intervals of 6 seconds, which may explain the ARC pattern.[5,6] Esophageal distension may also produce repetitive contractions. However, primary peristaltic contractions over a distended esophageal balloon are associated with swallow-induced primary and secondary peristaltic contractions proximal and distal to the balloon[22] and are linked with esophageal propulsive force proximal to the balloon.[21] In the absence of pressure data proximal and distal to the EndoFLIP, the relationship of the anterograde contractions, including ARCs, primary peristalsis, and secondary peristalsis, remains speculative and requires validation.

The ARC may represent a novel response to EndoFLIP,[2] possibly restricted to the distended balloon. However, no currently known neural circuit can explain repetitive primary or secondary peristalsis on the esophageal balloon. Balloon distension-induced contractions that are restricted to the balloon are nonpropagating spontaneous "tertiary: contractions[22] that are present as irregular, disorganized, and retrograde contractions.[4] The ARC pattern also does not resemble migrating motor complex in which the cluster of contractions moves as a group without any preceding inhibition. The ARC may represent a version of a normal motor pattern. Alternatively, the ARC may provide information on the propulsive force of the esophagus, either relevant to clearing the esophagus of food residues, obstructing solid bolus, or an interesting experimental finding relevant only to pressure dynamics in a fluid-filled obstructing esophageal balloon.[25] All these important hypotheses are testable and deserve to be validated.

Active marketing has led to the clinical use of EndoFLIP for the diagnosis of esophageal motility disorders. However, the results yielded by this technique are not based on the pathophysiologic understanding of esophageal motility disorders, and their significance is unknown. Therefore, the use of this inadequately evaluated,[26] expensive, and potentially risky technique for the investigation of esophageal motility disorders is not justified.

RAJ K. GOYAL
Division of Gastroenterology
Department of Medicine
Veterans Affairs Boston Healthcare System
West Roxbury, Massachusetts, *and*
Division of Gastroenterology, Hepatology, and Endoscopy
Department of Medicine
Beth Israel Deaconess Medical Center and Harvard Medical School
Boston, Massachusetts

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