The Spectrum of Motor Function Abnormalities in Gastroesophageal Reflux Disease and Barrett's Esophagus

D. Ang K. Blondeau D. Sifrim J. Tack

Department of Gastroenterology, University Hospital Gasthuisberg, Katholieke Universiteit Leuven, Leuven, Belgium

Key Words

Barrett's esophagus • Esophageal motility • Gastroesophageal reflux disease • Gastric intestinal metaplasia • Reflux esophagitis

Abstract

Barrett's esophagus has traditionally been regarded as the most severe end of the spectrum of gastroesophageal reflux disease and is of great clinical importance in view of the association with esophageal adenocarcinoma. Studies have documented high levels of esophageal acid exposure in Barrett's esophagus. Various pathogenetic mechanisms underlie this phenomenon. These include abnormalities in esophageal peristalsis, defective lower esophageal sphincter pressures, gastric dysmotility and bile reflux. Whilst these factors provide evidence for an acquired cause of Barrett's esophagus, an underlying genetic predisposition cannot be ruled out. Although the past decade has brought about many new discoveries in the pathogenesis of Barrett's esophagus, it has also added further controversy to this complex disorder. A detailed analysis of the gastrointestinal motor abnormalities occurring in Barrett's esophagus follows, with a review of the currently available literature and an update on this condition that continues to be of interest to the gastroenterologist.

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Introduction

Barrett's esophagus represents the most severe end of the spectrum of gastroesophageal reflux disease (GERD) [1] and is the most important risk factor for the subsequent development of esophageal carcinoma [2]. The pathogenesis of GERD is multifactorial [3]. GERD arises not from a single underlying pathology, but from a combination of anatomical and physiological causes [4]. These include abnormalities of the antireflux barrier at the gastroesophageal junction, impaired esophageal peristalsis resulting in abnormal clearance of the refluxate, gastric factors and duodenal gastro-esophageal reflux (DGER). As Barrett's esophagus forms the extreme end of the GERD spectrum, the pathophysiological mechanisms underlying severe reflux esophagitis and Barrett's esophagus are thought to be similar. Whilst motility abnormalities are commonly implicated in Barrett's esophagus, it remains controversial whether such abnormalities are the cause or the sequelae of severe reflux disease. Besides the commonly cited abnormalities in esophageal peristalsis and lower esophageal sphincter (LES) dysfunction, regional abnormalities in gastric motility and DGER which results in bile reflux [5] have been implicated in the pathogenesis of Barrett's esophagus. In this article, we review the currently available literature on the

Fig. 1. Spectrum of esophageal motor dysfunction in GERD patients. The graphs show findings in healthy controls (n = 70), functional heartburn (FH) (n = 64), non-erosive reflux disease (NERD) (n = 118), erosive reflux disease (ERD) (n = 88), ulcerative esophagitis (UE) (n = 31), short-segment Barrett's esophagus (SSBE) (n = 32) and long-segment Barrett's esophagus (LSBE) (n = 18). **a** Mean resting LES pressure. **b** Distal esophageal contractile amplitude. Numbers derived from Frazzoni et al. [16].

motility abnormalities in Barrett's esophagus, with emphasis on the LES, esophageal body and stomach and the controversial role of DGER (table 1).

Lower Esophageal Sphincter

The antireflux barrier at the gastroesophageal junction serves to prevent the occurrence of gastroesophageal reflux. The LES is the major component of this antireflux barrier and plays an important role in the pathogenesis of GERD. Low resting LES pressures have been found to correlate inversely with the severity of esophagitis, with pressures of <10 mm Hg reported in patients with severe reflux esophagitis [6]. An LES pressure of <6 mm Hg was associated with an increased likelihood of developing Barrett's esophagus (odds ratio of 2.9; 95% confidence interval 1.6–5.6) [7]. Several studies have documented lower mean basal LES pressures in patients with Barrett's esophagus compared to patients with uncomplicated GERD (fig. 1a) [8–16]. However, when patients with Barrett's esophagus are compared to patients with severe reflux esophagitis only, no significant differences in LES pressures were noted [17–20]. One study [19] has further evaluated the differences in manometric profile in Barrett's esophagus patients with or without associated erosive esophagitis. In this study, a reduced LES basal pres-

Table 1. Summary of esophageal motor abnormalities associated with Barrett's esophagus

Segment	Abnormality in Barrett's esophagus
Esophageal body	Decreased peristaltic amplitude Prolonged acid clearance
Lower esophageal sphincter (LES)	Low mean basal LES pressure
Gastroesophageal junction	Presence of a hiatal hernia
Stomach	Increased duodenogastric reflux Delayed gastric emptying?

sure and increased occurrence of deglutitions without motor response were noted in Barrett's esophagus patients who had associated erosive esophagitis compared to the group of Barrett's esophagus patients without associated esophagitis. These findings suggest that changes in the esophageal motility may reflect the inflammation of the esophageal wall rather than epithelial replacement [19]. The occurrence of lower impedance values at the LES in patients with erosive esophagitis and Barrett's esophagus compared to controls has been attributed to both changes in epithelial conductivity and to lower LES pressures affecting the mucosal contact with the imped-

ance electrodes [21]. It remains controversial whether the reduced LES pressure predisposes to excessive reflux or is secondary to chronic reflux damage and resulting weakness of the esophageal musculature [3].

The predominant mechanism of gastroesophageal reflux in both normal subjects and patients with reflux esophagitis is by transient lower esophageal sphincter relaxation (TLESR), first described in the 1980s by Dent and Dodds [22, 23]. Similar to patients with varying degrees of GERD including severe peptic esophagitis, TLESRs have also been shown to contribute to the occurrence of reflux in patients with Barrett's esophagus [24, 25]. However, the proportion of reflux episodes associated with TLESRs is inversely related to the degree of reflux esophagitis [25], but still constitutes 48–82% of reflux episodes [25–27]. The proportion of TLESRs in Barrett's esophagus compared to erosive esophagitis is, however, unknown. In such cases, a reduced basal LES pressure is the second most important mechanism of reflux [25].

Hiatal Hernia

A strong association has been described between the presence of a hiatus hernia and Barrett's esophagus [13, 28–32], with a 2-cm or longer hernia found in 96% of 46 patients with Barrett's esophagus [31]. Hiatal hernia impairs LES function [33], and the resultant lower LES pressure increases susceptibility to reflux events [34, 35]. In the presence of a hiatal hernia, the close apposition of the LES and the crural diaphragm is lost. Normally, a strong contraction of the crural diaphragm will prevent reflux during deep inspiration, straining or coughing [36, 37]. This contraction, which occurs faster than the increase of abdominal pressure [37], provides an active protection against straining-induced reflux, which is defective in case of a hiatal hernia [38]. In addition, a hiatal hernia may be associated with enhanced triggering of TLESRs [39]. Furthermore, the hiatal hernia pouch, which lies between the high-pressure LES proximally and the high-pressure diaphragmatic crural distally, may serve as a reservoir for the acidic gastric refluxate, where the acid refluxate is trapped in the hiatal hernia pouch during esophageal acid clearance and refluxes back into the esophagus during a TLESR or swallow-induced LES relaxation. Finally, during a TLESR the amount of refluxate will also be higher in a patient with a hiatal hernia because the distensibility of the gastroesophageal junction is increased and the flow over the junction is faster [40].

Esophageal Dysmotility

The esophageal body is a major component of the antireflux mechanism [41]. Peristalsis is essential for volume clearance of the esophageal bolus [42] and for delivery of the swallowed saliva to the distal esophagus [43]. This allows for respectively effective volume and chemical clearance of the refluxate. Acid clearance is a two-step process: swallowing and primary peristalsis aids in the transport of alkaline saliva to the distal esophagus, whilst secondary peristalsis is necessary for the clearance of the bulk of the refluxate. A longer delay from the onset of the reflux event to the initial clearing event has been shown in patients with reflux disease compared to controls [44]. Barham et al. [45] reported even longer acid clearance time in patients with reflux strictures. When compared to patients with all degrees of reflux esophagitis but without Barrett's esophagus, patients with Barrett's esophagus had longer acid clearance times [8, 18, 19] and increased numbers of reflux episodes [8, 19].

The impaired acid clearance has been ascribed to abnormalities in both primary and secondary peristalsis in reflux patients [3, 41]. Primary peristalsis is the initial response to acid reflux in normal subjects when in the upright position, whereas secondary peristalsis is the initial clearing event when subjects are supine and asleep [22, 23, 44, 46, 47]. Impairment of primary peristalsis is evident by the increased time to onset of the peristaltic response, fewer number of peristaltic events, increased time interval between peristaltic events, low-amplitude peristaltic contractions, simultaneous contractions and a lower number of complete peristaltic sequences in reflux patients compared to healthy subjects [45, 46, 48]. In addition, esophageal distension fails to trigger secondary peristaltic contractions in GERD patients [49].

Ineffective esophageal motility (IEM) is defined as distal esophageal contraction amplitudes (measured at 3 or 8 cm above the LES) of <30 mm Hg or non-transmitted contractions (peristaltic dropout at either 3 or 8 cm above the LES) $\geq 30\%$ of swallows [50], with one study reporting an overall incidence of IEM of 49% in GERD patients [51]. Studies have shown that mean pressure wave amplitudes in patients with Barrett's esophagus are lower than in normal subjects and in patients with mild reflux esophagitis [6, 11–18, 20, 52, 53] (fig. 1b). A pressure wave amplitude of at least 30 mm Hg is required for effective reflux volume clearance [25]. The frequency of peristaltic dysfunction has been shown to rise with the severity of reflux disease, ranging from 25% in patients with mild reflux esophagitis and to 48% in patients with

severe esophagitis [42]. The prevalence of IEM in Barrett's esophagus has not been specifically studied.

In view of the evidence showing impaired esophageal peristalsis and longer esophageal clearance times in patients with severe reflux esophagitis and Barrett's esophagus, it is not surprising that these patients are subjected to the highest levels of esophageal acid exposure [8, 54, 55]. Nevertheless, whether esophageal peristaltic dysfunction is a primary defect independent of mucosal changes, or arises from reflux-induced mucosal injury with resultant esophageal dysmotility is still a matter of controversy. In the studies that were conducted evaluating esophageal amplitudes at various locations along the esophagus, the reduction in esophageal peristaltic wave amplitudes was not seen in the proximal esophagus [6, 17, 18, 20], an area where exposure to acid reflux is rare. This suggests that dysmotility may arise secondary to reflux disease. However, the control of peristalsis and the underlying muscular mechanisms differ strongly between proximal and distal esophagus, and these anatomical and physiological differences could also explain why both parts are differentially affected. Studies assessing the effects of healing of esophagitis on esophageal motility have yielded inconsistent results. Improvement in esophageal contractility and LES pressure has been occasionally reported with acid suppressive therapy [56–58] and also from surgical series [59–61]. An increase in the amplitude of esophageal contractions and a corresponding decrease in the number of ineffective swallows was documented on manometry in patients after a median follow-up of 3.5 years after Nissen fundoplication [59]. Sagar et al. [60] reported a significant improvement in LES pressure after fundoplication, with 24 of 56 patients showing partial or complete regression of Barrett's esophagus. Ireland et al. [61] reported two major effects of fundoplication: a 50% reduction in the rate of TLESRs and a reduction in the proportion of TLESRs that were accompanied by reflux from 46 to 17%. Nevertheless, such improvement in LES pressure may simply represent the effects of the artificial high-pressure zone that was created around the LES by fundoplication, and which persists during both transient and swallow-induced LES relaxation [62]. On the other hand, large studies did not show that healing of esophagitis with either histamine type-2 receptor antagonists or proton pump inhibitors affected LES pressure or esophageal peristaltic contractions [63–67]. Paired esophageal motility evaluation in 41 patients prior to and after photodynamic therapy for Barrett's high-grade dysplasia or esophageal adenocarcinoma revealed abnormal esophageal motility in 14 patients at baseline (3 patients

with diffuse esophageal spasm, 7 with IEM and 4 with aperistalsis). Following photodynamic therapy, 1 of 3 patients and 1 of 7 patients had resolution of diffuse esophageal spasm and IEM respectively [68]. These findings, although not statistically significant, represent the only study evaluating baseline and posttreatment esophageal motility in patients with Barrett's esophagus.

The length of the columnar lined mucosal has been shown to reflect the degree of esophageal damage, with a greater reduction of the peristaltic wave amplitude [11, 69] and a higher esophageal acid exposure in patients with long-segment Barrett's esophagus compared to short-segment Barrett's esophagus [69]. Review of the motility studies in 70 patients with Barrett's esophagus [70] showed a significantly longer duration of swallow-induced esophageal contractions and reduced amplitudes of esophageal contractions in patients with extended segment (>5 cm) compared to limited segment (3–5 cm) Barrett's esophagus, with the most marked changes seen in the distal esophagus.

An increased prevalence of dysphagia could be expected in Barrett's esophagus based on the poor esophageal motility described above. Comparative studies have confirmed a higher prevalence of dysphagia and more impaired esophageal bolus transport in Barrett's versus non-Barrett's GERD patients [71–73]. In addition, esophageal peptic ulcer or stricture are significantly more frequent among patients with 'long-segment' Barrett's esophagus, and this may also contribute to dysphagia symptom generation [74]. A matter of ongoing controversy is whether the poorer motility in Barrett's esophagus affects the occurrence of dysphagia after antireflux surgery. However, most publications fail to find increased postoperative dysphagia rates in Barrett's esophagus, in the absence of a reflux stricture [75–77].

Esophageal Sensitivity

As described above, patients with Barrett's esophagus are characterized by enhanced esophageal reflux exposure and by impaired esophageal motor function. Although similar abnormalities have been implicated in symptom generation in patients with erosive and non-erosive reflux disease, patients with Barrett's esophagus seem to have a similar or even decreased symptom burden compared to non-Barrett's GERD patients [13, 14, 78]. Studies using esophageal acid perfusion and balloon distention reported decreased sensitivity to these stimuli in patients with Barrett's esophagus, and this could con-

tribute to the lower symptom perception in these patients [79]. It is unclear whether impaired sensitivity is also contributing to impaired esophageal motility in Barrett's, but it is conceivable that impaired detection of bolus presence may contribute to poor primary and secondary peristalsis.

The mechanism underlying esophageal hyposensitivity in Barrett's has not been elucidated, but it has been proposed that the Barrett's mucosa was less sensitive to chemical stimuli, compared to the normal esophageal mucosa. Ambulatory pH monitoring studies confirmed that similar amounts of acid exposure were less likely to be perceived by Barrett's patients compared to GERD patients without Barrett's esophagus [80]. In the same study, the authors observed that abnormal motility in Barrett's esophagus was associated with longer acid contact times and a greater likelihood of symptom perception [80]. Whether altered tone and contractility of the esophageal body is also involved in decreased sensitivity has presently not been investigated.

Gastric Dysmotility

The role of delayed gastric emptying as a pathophysiological factor in patients with GERD is controversial. A number of studies have shown delayed gastric emptying in patients with GERD [80–85]. In theory, delayed gastric emptying could lead to accumulation of a larger intragastric volume of solids and liquids leading to reflux [86] or the resultant gastric distension may provoke more TLESRs [36, 87, 88], possibly through activation of gastric mechanoreceptors [37–39, 89, 90]. On the other hand, several studies have failed to show a correlation between delayed gastric emptying and increased gastroesophageal reflux. These studies reported either no delay in gastric emptying [91–93] or only infrequent delays [94, 95].

Even as studies on delayed gastric emptying have revealed conflicting results, its role in the development of GERD may be overestimated, as shown in a recent study of patients with endoscopy negative GERD where no relationship between cisapride-induced accelerated gastric emptying and decrease in esophageal acid exposure was reported [96]. Apart from abnormalities in gastric emptying, regional disturbances in gastric motility have also been implicated in the development of GERD, although conflicting results were reported. Most studies have reported either prolonged or abnormally enhanced postprandial gastric relaxation [97–99]. Similar to delayed gastric emptying, an abnormal increase in proximal gas-

tric relaxation leads to increased gastric distension and may increase the number of TLESRs. Studies specifically addressing the prevalence of delayed gastric emptying in Barrett's esophagus are lacking.

Many patients with GERD have concomitant dyspeptic symptoms [100–102], suggesting that these two entities may overlap. Contrary to the above-mentioned studies where gastric emptying was delayed in GERD patients, one study has reported increased proximal gastric emptying and decreased retention of a liquid nutrient meal in the proximal stomach of patients with GERD and concomitant dyspepsia [103]. These patients were also found to have a significant negative correlation between proximal gastric retention and the number of acidic reflux episodes. It is likely that the abnormal pattern of intragastric distribution of a liquid meal demonstrated in this study indicates the concomitant gastric motor disorders seen in patients with functional dyspepsia, who typically manifest decreased retention of food in the proximal stomach secondary to impaired accommodation [104–106]. These findings suggest that a different pathophysiology may be present when GERD and functional dyspepsia overlap.

Duodenal Gastroesophageal Reflux

The observation that Barrett's mucosa developed after total gastrectomy with esophagojejunostomy [107] suggests that acid reflux is not the only pathogenetic factor implicated in the genesis of Barrett's esophagus. Constituents of the refluxate have been shown to play a role in the pathogenesis of the columnar lined epithelium of the esophagus. Reflux of duodenal contents into the stomach and esophagus has been implicated in the pathogenesis of Barrett's esophagus and reflux esophagitis [54]. Bile acids and trypsin have been shown to cause injury to the esophageal mucosa in experimental animal models [108]. The available data suggest synergism between hydrochloric acid and conjugated bile acids at low pH, and between unconjugated bile acid and trypsin at neutral pH 7 [109]. However, difficulty exists in distinguishing the relative contributions of acid and duodenal contents within the refluxate. Reports based on static measurements of gastric and esophageal aspirates for analysis of bile acids are unphysiological, are usually measured over periods of hours rather than of single reflux episodes and require complex biochemical analysis [55, 110].

The advent of a 24-hour ambulatory bilirubin monitoring system which uses the optical property of bilirubin

pigment to detect bile (Bilitec 2000; Synectics) has led to increased interest in DGER [111]. This fiberoptic system quantifies absorption at the 450 nm spectrophotometric band, which is characteristic for bilirubin and represents DGER. Although this technique is relatively non-invasive, it merely detects the presence or absence of bilirubin as a marker of duodenal contents (bile salts, trypsin and lysolecithin). Its use in clinical practice is limited by a number of drawbacks such as the necessity to take a modified diet and the occurrence of food impaction artifacts that interfere with adequate measurements. However, when used in large groups of patients, Bilitec data can provide information with pathophysiological relevance.

Most studies of ambulatory bilirubin monitoring have combined Bilitec with pH monitoring, and are supportive of a synergistic effect of bile and acid reflux in the development of Barrett's esophagus [112–116]. Champion et al. [112] using simultaneous 24-hour pH and bile monitoring of the distal esophagus found a close association between total percent of time pH <4 and DGER, with the most severe DGER documented in patients with Barrett's esophagus. Similar findings were documented by Vaezi and Richter [113] where patients with complicated Barrett's esophagus had significantly greater amounts of both acid and bile reflux. In a multivariate model including acid, bile, age and gender dependency, only bile reflux was shown to correlate with less effective esophageal motility [117]. Taken together, these studies showed the most severe forms of esophagitis occurring in patients with a combination of severe reflux of acid and duodenal contents. It is unclear whether the higher DGER exposure in higher-grade lesions and in Barrett's esophagus merely reflects increased reflux events, as indicated by the higher acid exposure, or whether this is an independent factor contributing to the development of esophageal lesions. A multivariate analysis of the relationship between lesions and reflux patterns showed that, besides male sex, both acid exposure and DGER exposure are independent risk factors associated with the presence of Barrett's esophagus, suggesting a synergistic activity of acid and bile in inducing Barrett's mucosa [118].

The motility abnormalities underlying DGER are unknown, but may include disordered antroduodenal motility [94, 119], delayed gastric emptying and abnormalities of the LES. Reflux of duodenal contents into the stomach is a physiological phenomenon, which occurs in health after a meal [120]. However, an excessive amount of reflux of duodenal contents to the stomach may be pathological. Bile reflux gastritis can occur after any surgical procedure which affects the sphincteric properties

of the pylorus, most commonly seen after distal gastrectomy with a Bilroth II gastrojejunostomy [121]. In the absence of surgery, pyloric incompetence has been postulated to be attributed to intrinsic antropyloroduodenal incoordination [3], a mechanism that requires further research. Whilst ambulatory esophageal bilirubin monitoring favors a role for DGER in causing GERD, it is unclear if this is accompanied by a similar increase in duodenogastric reflux (DGR). Prior studies using scintigraphy yielded conflicting results, with increased DGR documented in patients with Barrett's esophagus in some studies [122, 123], but unrelated to GERD severity in another [124]. Aspiration studies showed higher fasting bile acid concentrations in the stomach in patients with Barrett's esophagus compared to controls or esophagitis patients, and patients with complicated Barrett's esophagus had the highest fasting bile acid concentrations [114]. These studies suggest abnormal DGR, or impaired bile clearance from the stomach in Barrett's patients. In contrast, in a study by Marshall et al. [125] using combined ambulatory esophageal and gastric pH and gastric bilirubin monitoring in healthy subjects and GERD patients with varying severity, DGR was not shown to parallel DGER. Comparison of 24-hour esophageal and gastric pH and gastric bilirubin in patients with uncomplicated GERD, GERD with erosive esophagitis, uncomplicated Barrett's esophagus and healthy controls revealed no significant difference in gastric bilirubin exposure in the four groups, whilst acid reflux increased from healthy subjects up to patients with esophagitis and Barrett's esophagus. These findings suggest that esophageal exposure to duodenal contents in GERD may rely on factors that influence acid exposure, namely the competence of the LES and esophageal clearance mechanisms rather than on disordered gastroduodenal motility.

Development of Columnar Mucosa after Esophagectomy

Barrett's esophagus has been reported to arise de novo in patients who have previously undergone gastric pull-up esophagectomy [126–131]. In this procedure, the normal squamous epithelium of the cervical esophagus is interposed to the acid secreting mucosa of the gastric body. Histopathology studies reviewed the presence of cardiac type mucosa at the surgically created esophago-gastrostomy site and the development of Barrett's mucosa has been documented in pathological series. These findings are consistent with the proposal that in the set-

ting of persistent gastroesophageal reflux, denudation of the squamous epithelium above the anastomotic site is followed by migration of immature cells derived from the gastric fundic mucosa and subsequent differentiation into Barrett's mucosa occurs [129]. It remains controversial whether Barrett's esophagus occurs from a congenital or acquired cause. The presence of pre-existing Barrett's esophagus prior to surgery was the most important factor determining the development of postoperative intestinal metaplasia [127], lending support to an underlying genetic predisposition [130, 131]. Conversely, the duration of reflux symptoms rather than preexisting intestinal metaplasia was found to correlate with the development of postoperative Barrett's esophagus [130] providing evidence for an acquired etiology.

Relationship between Barrett's Esophagus and Other Disorders Associated with Motility Disorders of the Gastrointestinal Tract

Barrett's esophagus has been associated with other motility disorders of the gastrointestinal tract, namely scleroderma [132–134] and celiac disease. Severity and extent of reflux has been attributed to the integrity of distal esophageal peristalsis. Murphy et al. [133] found a significantly lower number of reflux events, but they were of longer duration when patients with manometric features of scleroderma and endoscopic findings of esophageal ulcerations and/or Barrett's esophagus were compared to patients with similar endoscopic findings but without an associated connective tissue disorder. Based on their findings, they concluded that decreased smooth muscle peristalsis was attributed to be the primary contributor of esophageal injury in scleroderma. However, in a study by Katzka et al. [134], who reported a 38% occurrence of Barrett's esophagus in scleroderma patients, no significant differences were found in the manometric profile in patients with or without associated Barrett's esophagus. Yarze et al. [135] found that by linear regression analysis, there was a poor correlation between the severity of esophageal acid exposure and the LES pressure. They postulated that the severity and extent of GER in scleroderma is most closely related to the integrity of distal esophageal peristalsis.

An increased prevalence of specialized intestinal metaplasia has been observed in esophageal biopsy specimens of untreated celiac patients, both in children [136] and in adults [137]. Maieron et al. [137] noted increased rates of Barrett's esophagus in 26.6% of untreated adult

celiac disease patients, compared to 10.9% of controls undergoing endoscopy for other reasons. These findings may be due to the gastric and LES motor abnormalities [138] leading to chronic reflux in patients with celiac disease, combined with a mucosa sensitive to gliadin. Furthermore, gut transit has been shown to be delayed in celiac disease, as was observed in the small bowel of untreated male patients, with a significant acceleration of small bowel transit time observed after institution of a gluten free diet [139].

Conclusion

Disturbed motility has been shown in patients with Barrett's esophagus (table 1). As illustrated above, these motility abnormalities span the upper gastrointestinal tract. However, the prevalence of esophageal manometric abnormalities in Barrett's esophagus and the impact of medical or surgical treatment on the motility abnormalities seen in Barrett's esophagus remain poorly studied. Whether gastroesophageal reflux results in a progressive deterioration of motility or whether an initial poor motility results in prolonged acid exposure remains uncertain. No study to date has followed the changing pattern of motility in Barrett's esophagus over time.

Current treatment options for Barrett's esophagus include antireflux therapy (medical or surgical) in patients with reflux symptoms and esophagectomy for adenocarcinoma. Novel endoscopic techniques have been described for high-grade dysplasia. The impact of these treatment options on motility abnormalities in Barrett's esophagus is not well established. Preliminary evidence from one study [68] suggests that esophageal motility abnormalities can resolve after treatment with photodynamic therapy, but these findings were not statistically significant. Conventional acid suppressive therapy with H₂-receptor antagonists or proton pump inhibitor therapy does not stop the reflux of gastric contents, and failure of symptoms to respond to acid reduction may be attributed to the presence of duodenal contents in the refluxate causing an unabated injury to the esophagus with its associated motility abnormalities. We await further discoveries into the pathogenesis of this complex disorder.

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