The acid pocket, hiatal hernia and TLESRs: essential players in the pathogenesis of gastro-esophageal reflux disease
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Stepwise radiofrequency ablation of Barrett’s esophagus preserves esophageal inner diameter, compliance and motility

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Abstract

Background and aim: Stepwise endoscopic circumferential and focal radiofrequency (RF) ablation is safe and effective for the eradication of Barrett’s esophagus (BE). In contrast to other techniques, RF ablation appears to avoid significant esophageal scarring or stenosis. Our aim was to evaluate whether RF ablation has an adverse effect on esophageal function in patients treated for BE containing intramucosal cancer (IMC) and/or high-grade dysplasia (HGD).

Methods: Twelve patients with BE containing IMC or HGD were included. After endoscopic resection of visible abnormalities, stepwise circumferential and focal ablation were performed every 2 months up to a maximum of 5 sessions. Measurement of the inner diameter was performed at 1 cm intervals in the distal esophagus. Manometry was performed using water-perfused sleeve catheter. Compliance was evaluated using the functional luminal imaging probe (FLIP), measuring 8 cross sectional areas within a saline-filled bag with 2 pressure side holes; one proximal to and one inside the bag. Esophageal sizing, manometry and compliance were recorded in patients at baseline and at least 2 months after the final ablation session. In addition, FLIP and manometry measurements were performed in 10 healthy volunteers.

Results: All patients achieved complete eradication of dysplasia and BE, without severe complications or ablation related stenoses. The esophageal diameter was unchanged by the ablation. Lower esophageal sphincter (LES) pressure, LES length and esophageal contraction amplitude were not significantly different before and after ablation. Baseline compliance was significantly different between healthy volunteers and BE patients. Compliance did not, however, change significantly in patients before and after ablation.

Conclusions: Stepwise circumferential and focal ablation of BE is an effective and safe treatment modality for early Barrett’s neoplasia that appears to preserve the esophageal functional characteristics.
Introduction

Barrett’s esophagus (BE) is a premalignant condition, which increases the risk of developing esophageal adenocarcinoma. Patients with a known BE are advised to undergo regular endoscopic surveillance in order to detect neoplastic lesions at an early and curable stage. Until recently, esophagectomy was considered the treatment of choice in BE patients with the early neoplastic lesions of high grade dysplasia (HGD) and intramucosal carcinoma (IMC). This surgery, however, is associated with significant mortality and morbidity even in high-volume centres. Endoscopic treatment has recently emerged as a safe and effective alternative to surgery for selected patients with early Barrett’s neoplasia. Endoscopic treatment techniques can be divided into two distinct categories: endoscopic resection (ER) and endoscopic ablation. ER allows for the removal of focal lesions enabling their histological evaluation. When used as monotherapy, however, ER may be associated with subsequent formation of new neoplastic lesions within the unresected Barrett’s segment. Therefore, after removal of the early neoplastic lesions, the remainder of the Barrett’s mucosa should ideally be removed as well, either by additional sessions of ER or by ablative techniques such as photodynamic therapy (PDT) and argon plasma coagulation (APC). Drawbacks of these techniques, however, include esophageal scar and stricture formation, the development of dysphagia, poor ablative depth control and difficulty with ease of use. In our previous series, 26% of patients who underwent complete resection of BE using stepwise radical ER developed a symptomatic esophageal stenosis and a 30% stenosis rate has been reported after Photofrin-PDT.

Recently, our group has prospectively investigated the efficacy of a relatively new ablation technique, stepwise circumferential and focal radiofrequency ablation using the HALO-system, for BE with early neoplasia. With this technique, the Barrett’s mucosa is ablated by radiofrequency energy delivered through a balloon-based electrode for circumferential ablation (HALO360) or a cap based catheter for focal ablation (HALO90). In contrast to previous ablation techniques, the energy is delivered to the superficial mucosal layer, a feature which is crucial to reduce scar formation thereby preventing subsequent stenosis and/or dysphagia. In our studies, complete eradication of neoplasia and complete removal of BE was achieved in all patients, with no post-ablation esophageal stenosis or dysphagia. Transport of the ingested bolus through the esophagus not only depends on propulsive forces generated by esophageal peristalsis. Parameters such as distensibility, opening patterns of the lower esophageal sphincter and the diameter of the esophagus are also important. To evaluate the effect of new therapeutic interventions for early BE neoplasia on esophageal function, objective assessment of these parameters is clinically relevant in order to guide our choice of treatment. At present, esophageal manometry still represents the gold standard to evaluate peristalsis and measure relaxation of the lower esophageal sphincter. However, manometry fails to evaluate bolus transit, and provides no information on impaired distensibility or reduced diameter of the esophagus, for example in case of scarring. Recently, a new technique has been developed and validated to measure the compliance or distensibility upon radial expansion of the esophagus. On the basis of
impedance planimetry, an already established technique for performing bag distensions in the gastrointestinal tract\textsuperscript{12-14}, a functional lumen imaging probe (FLIP) has been constructed that measures the cross sectional areas (CSA) at several sites in a saline-filled bag. Previous studies have shown FLIP to be useful in measuring changes in distensibility of the esophagogastric junction (EGJ) in healthy volunteers, gastro-esophageal reflux disease patients, and patients with achalasia.\textsuperscript{9, 15} Therefore, we used FLIP, together with manometry and a purpose-designed device measuring the diameter of the esophagus during the endoscopic procedure, to study whether esophageal function is hampered by BE ablation using the HALO system. In addition, we compared our manometry and compliance data with those obtained from healthy subjects.

**Materials and Methods**

**Subjects**

Ten healthy asymptomatic volunteers (7 males, median (IQR) age 22 yrs (21-48)) and twelve patients (9 males, median (IQR) age 70 yrs (52-76)) were studied. None of the volunteers had a history of previous upper gastrointestinal surgery or were taking any medication. Volunteers were recruited by public advertisement. Details on the patient selection criteria have been published in this journal.\textsuperscript{7} In short, patients were eligible for ablative therapy if they had a BE with a length between 2 and 12 cm and HGD or IMC diagnosed at two separate endoscopies. All patients with endoscopically visible abnormalities had these lesions removed by ER prior to ablation, to stage the lesion and ensure that ablation was performed on an endoscopically flat mucosa. The study was approved by the Medical Ethical Committee of the Academic Medical Centre and written informed consent was obtained from all participants.

**Endoscopy**

Primary circumferential ablation was performed with a balloon based electrode using 2 applications of 12 J/cm\textsuperscript{2}. Subsequent ablation sessions were scheduled at 2 months intervals. For isolated BE islands with a maximum length of 2 cm and less than 50% of the circumference, secondary focal ablation was performed with an endoscope-mounted ablation device. Larger residual areas of BE were treated with secondary circumferential ablation. A maximum of 2 circumferential and 3 focal ablation sessions were allowed. Two months after the last treatment session, endoscopy with narrow band imaging was performed to evaluate the presence of residual BE. If no residual BE was present, random biopsies (4Q Bx/1cm) were obtained from neo-squamous epithelium throughout the full extent of the original BE, and from the area immediately distal to the neo-squamocolumnar junction. If residual BE was evident after the maximum number of ablation sessions, a focal ER using the multi-band mucosectomy technique was performed as “escape treatment”, with endoscopy and biopsy performed two months later.
Esophageal function after mucosal ablation

Esophageal inner diameter sizing
In order to assess the inner esophageal diameter, we used a non-compliant balloon catheter associated with the sizing component of the HALO system (BÂRRx Inc., Sunnyvale, CA, USA). Upon activation, the balloon is automatically inflated to 4 psi (0.28 atm) and the internal esophageal diameter is automatically calculated based on baseline balloon volume/geometry and the inflated pressure/volume. Subsequently, the balloon is automatically deflated. The HALO360 sizing balloon can measure esophageal diameters in the range of 18 to 33.7 mm and each measuring cycle takes approximately 6 seconds. Measurements were performed with 1-cm intervals of at least the distal 10 cm of the esophagus. Esophageal diameters were measured at the first ablation session before treatment and two months after the final treatment procedure.

Compliance measurement of the distal esophagus
Distensibility of the distal esophagus, just above the EGJ, was measured using the FLIP, custom designed to measure 8 cross sectional areas (CSAs) under radial stretch and containing 2 manometric pressure side holes (Figure 1). The distal end of the probe, constructed of a polyethylene tube with an outer diameter of 1.6 mm, is surrounded by a 10 cm long, oversized bag that would contact the esophageal wall upon inflation. An excitation current of 100 µA at a frequency of 5 KHz, was generated between two excitation electrodes located on each side of the multiple detection electrodes. Voltage measurements were made across 8 electrode pairs. Each electrode in the pair was 1 mm apart and the distance between the centres of the electrode pairs, i.e. the distance between the measurements, was 4 mm. The voltage measured was proportional to the impedance between the detection electrodes, which decreased as the bag filled with saline. This impedance change was therefore proportional to the CSA change at each detection electrode pair in the bag. The bag filled without resistance up to its maximum distending volume, so that any pressure increase recorded in the bag did not reflect distensibility of the bag. The bag ends were folded in before being fixed to the

Figure 1. The functional lumen imaging probe (FLIP).

Distal end of 8 CSAs probe showing electrode arrangement inside the bag. Also shown are the signals channels, fill and perfusion channels at the proximal end (McMahon et al. Phys. Meas. 2005).
probe, creating a rolling-bag effect, which allowed some longitudinally movement of the bag without dislodging the bag. Pressure measurements were performed proximal to and inside the bag, using a low compliance saline perfused system connected to external transducers. Pressure and CSA were recorded at a rate of 10 Hz.

Prior to each study, a set of perspex cylindrical tubes with CSAs between 38.5 mm² and 572 mm² was used to calibrate the FLIP. Calibration was performed with 0.225 g/l saline at body temperature. The pressure system was calibrated at 0 and 100 cm H₂O. After anaesthetising the throat, the FLIP was inserted orally and positioned with the bag 1-2 cm above the EGJ, using manometry readings of the proximal side hole and point of respiratory inversion as a guide. At least two preconditioning distensions were performed by infusing the bag with 0.225 g/l saline. In addition, two volume controlled distensions at 25 ml/min were carried out to a maximum of 60 ml or stopped earlier in the case of discomfort. During the distensions, patients were asked to refrain from swallowing. Studies were performed in the semi-recumbent position.

Compliance of the distal esophagus was measured as cross sectional area at the narrowest point plotted against bag pressure. This compliance data was captured during the bag distension at 25 ml/min. For every 10ml-step volume, the narrowest CSA and its corresponding pressure were assessed.

FLIP studies were performed prior to ablation treatment, at least 6 weeks after any prior ER, and post-treatment at 2 months after the last treatment session.

**Esophageal manometry**

Esophageal manometry was performed using a 10-lumen assembly (Dentsleeve, Adelaide, Australia) with a sleeve sensor incorporated at its distal end to monitor lower esophageal sphincter (LES) pressure. Side holes monitored pressure in the stomach (1 cm below the distal margin of the sleeve) and at 2, 5, 8, 11, 14, 17 and 20 cm above the LES. A side hole in the pharynx monitored swallows. The side holes and the sleeve were perfused with degassed distilled water at 0.6 ml/min, using a pneumohydraulic capillary perfusion pump (Dentsleeve Pty, Belair, South Australia). Pressures were sensed by external transducers connected to a polygraph (Medtronic Synectics Medical, Stockholm, Sweden).

The manometric catheter was introduced through an anaesthetised nostril and positioned so that the sleeve straddled the LES. After a period of baseline recordings, ten 5 ml water swallows were given at 20 s intervals to assess peristaltic function. Studies were performed with the subjects in the right lateral position.

Esophageal manometry was performed prior to ablation, at least 6 weeks after any prior ER, and post-treatment at 2 months after the last treatment session.

**Study protocol**

After the endoscopic work-up (with or without ER for removal of visible lesions), patients underwent esophageal manometry and compliance measurements using the FLIP technique. In addition, the esophageal diameter was measured and the first ablation session was
performed. This ablation was performed within 3 months after the last mapping endoscopy and, in case of a prior ER, after a minimum period of 6 weeks after the ER. Two months after the last treatment session the outcome parameters were again assessed, followed by endoscopy with narrow band imaging to evaluate the presence of residual Barrett’s mucosa and measurement of esophageal diameter.

In addition to the patients studied, compliance measurements and manometry were also performed in ten healthy subjects without any gastrointestinal symptoms.

**Data analysis and statistics**

The sizing results before and after ablation were compared as follows: all pre- and post-treatment measurements were grouped in pairs based on the insertion depth of the sizing balloon. The widening of the esophagus into the hiatal hernia was used as an internal control to ensure that the diameter values were compared at the same level. For each level at which the sizing procedure was performed before and after treatment, the difference in the measured internal esophageal diameter was calculated. The null hypothesis was that the median difference for all inner esophageal diameter comparisons would not be significantly different from zero. We used the Wilcoxon rank sum test to test this hypothesis using a significance level of 0.05.

LES length was determined manometrically using the station pull through technique. Basal LES pressure was measured at end-expiration relative to intragastric pressure. Peristaltic wave amplitudes were measured by averaging baseline to peak pressures for the proximal (17 and 20 cm above the LES), mid (11 and 14 cm above the LES) and distal (2, 5 and 8 cm above the LES) esophagus. Peristalsis was defined as normal when a wet swallow was propagated as an un-interrupted, peristaltic wave contraction, with amplitudes exceeding 15mmHg in the proximal esophagus and above 25mmHg in the mid and distal esophagus. Manometry and compliance data are presented as mean ± SEM in case of a normal distribution and as median (25%-75%) for variables with a skewed distribution. Where appropriate, statistical analysis was done using the Student’s T-tests, the Wilcoxon rank sum test or the Mann-Whitney test all using paired testing. A P-value < 0.05 was regarded as statistically significant.

**Results**

**Clinical results**

Twelve patients (9 males, median (IQR) age 70 yrs (52-76)) were included. The median length of the Barrett’s segment was 7 cm (6.5-8 cm). Seven patients underwent ER for focal removal of visible abnormalities prior to ablation (six piecemeal resections, median number of 2 resections (IQR 2-3)). The worst pathological grade after ER and prior to ablation was LGD (n = 1) and HGD (n = 11). Details on the treatment outcome of these patients have been published in this journal. In summary, after a median number of 1 HALO360 sessions and 2
HALO90 sessions, all patients had complete eradication of HGD and IMC as well as complete endoscopic and histological removal of all IM (including biopsies from neosquamous mucosa and biopsies obtained immediately distal to the neo-squamocolumnar junction) (Figure 2). Two patients underwent focal ER after ablation therapy. In one patient, a circumferential ablation was combined with a focal ER because a small nodule was encountered. This patient subsequently developed a symptomatic stenosis at the ER site, which was effectively resolved with a single endoscopic dilation. In the second patient, residual Barrett’s mucosa persisted after the maximum allowed ablative sessions, and was then removed with ER. Both patients were excluded from further functional testing since intervening ER may confound the follow-up functional measurements.

**Esophageal sizing**

For each inner esophageal diameter measurement session, a medium number of 12 measurements were obtained (IQR: 7-18). Narrowing of the inner diameter was not observed after ablation. The median esophageal diameter before and after treatment was 31.5 mm and 31.3 mm, respectively (P = 0.87). The median difference in paired diameter values per patient per level before and after treatment was 0.5 mm (IQR: 0.28-0.93) (P = 0.13) (Table 1).

**Manometry**

Manometry was performed in eight healthy volunteers and in seven patients pre and post ablation. Two healthy volunteers refused to undergo the procedure, and in three patients manometry insertions failed (n = 1) or patients refused to undergo the procedure after completing the treatment protocol (n = 2).

In healthy subjects, the median LES resting pressure was 9.0 (4.5-13.3) mmHg. This was significantly higher compared to patients before ablation treatment (4.0 (2.0-5.0) mmHg, P = 0.02), but not compared to patients after ablation (4.0 (3.0-8.0) mmHg, P = 0.9) (Table 2). There were, however, no significant differences in the median LES pressure measured before and after ablation (P = 0.10).
The median LES length was found to be significantly greater in healthy volunteers than in patients (HV: 4.0 (3.0-4.8) cm; pre-ablation: 2.0 (2.0-3.0) cm, P = 0.009 compared to HV; post-ablation: 2.0 (2.0-3.0) cm, P = 0.005 compared to HV) (Table 2). The median LES length was, however not significantly different before and after ablation.

The amplitude of the peristaltic contraction waves was measured in the proximal, mid and distal esophagus and did not differ significantly before and after ablation therapy. For the proximal esophagus, there was no significant difference in contraction amplitude between healthy subjects and BE patients. However, the contraction amplitude in the mid esophagus was significant higher in healthy volunteers compared to BE patients (HV; 61 ± 8 mmHg; pre-ablation: 27 ± 4 mmHg, P = 0.001 compared to HV: post-ablation: 29 ± 4 mmHg, P = 0.002 compared to HV). In the distal esophagus, the contraction amplitude in healthy volunteers was 70 ± 6 mmHg. This was significantly higher compared to patients before

Table 1: Oesophageal diameter (ED) in patients with early Barrett’s neoplasia before and after HALO ablation.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Pre-ablation ED (mm)</th>
<th>Post-ablation ED (mm)</th>
<th>Δ in mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>31.4</td>
<td>32.3</td>
<td>0.9</td>
</tr>
<tr>
<td>2</td>
<td>23.9</td>
<td>25.4</td>
<td>0.5</td>
</tr>
<tr>
<td>3</td>
<td>32.2</td>
<td>31.8</td>
<td>0.4</td>
</tr>
<tr>
<td>4</td>
<td>31.5</td>
<td>30.7</td>
<td>0.8</td>
</tr>
<tr>
<td>5</td>
<td>33.0</td>
<td>32.0</td>
<td>1.0</td>
</tr>
<tr>
<td>6</td>
<td>25.2</td>
<td>25.7</td>
<td>0.5</td>
</tr>
<tr>
<td>7</td>
<td>30.2</td>
<td>28.7</td>
<td>1.5</td>
</tr>
<tr>
<td>8</td>
<td>25.3</td>
<td>25.8</td>
<td>0.3</td>
</tr>
<tr>
<td>9</td>
<td>32.8</td>
<td>32.6</td>
<td>0.2</td>
</tr>
<tr>
<td>10</td>
<td>32.2</td>
<td>32.2</td>
<td>0.0</td>
</tr>
<tr>
<td>median</td>
<td>31.5</td>
<td>31.3</td>
<td>0.5</td>
</tr>
<tr>
<td>25%-75%</td>
<td>25.3-32.4</td>
<td>25.8-32.2</td>
<td>0.28-0.93</td>
</tr>
<tr>
<td>mean</td>
<td>29.8</td>
<td>29.7</td>
<td>0.6</td>
</tr>
<tr>
<td>p</td>
<td>0.87</td>
<td></td>
<td>0.13</td>
</tr>
</tbody>
</table>

Table 2: Oesophageal manometry in patients with early Barrett’s neoplasia before and after HALO ablation and in healthy volunteers.

<table>
<thead>
<tr>
<th></th>
<th>Pre-ablation</th>
<th>Post-ablation</th>
<th>HV</th>
</tr>
</thead>
<tbody>
<tr>
<td>LES pressure (median, IQR)</td>
<td>4.0 (2.0-5.0) *</td>
<td>4.0 (3.0-8.0)</td>
<td>9.0 (4.5-13.3)</td>
</tr>
<tr>
<td>LES length (cm; median, IQR)</td>
<td>2.0 (2.0-3.0) *</td>
<td>2.0 (2.0-3.0) *</td>
<td>4.0 (3.0-4.8)</td>
</tr>
<tr>
<td>Contraction amplitude (mmHg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proximal oesophagus</td>
<td>42.0 ±10.2</td>
<td>49.5 ± 8.9</td>
<td>47.3 ± 5.1</td>
</tr>
<tr>
<td>Mid oesophagus</td>
<td>26.7 ± 3.9 *</td>
<td>29.1 ± 4.1 *</td>
<td>60.9 ± 8.2</td>
</tr>
<tr>
<td>Distal oesophagus</td>
<td>48.9 ± 7.3 *</td>
<td>57.7 ± 8.0</td>
<td>70.0 ± 6.1</td>
</tr>
<tr>
<td>Normal peristalsis (%)</td>
<td>64.3 ± 16.3</td>
<td>71.4 ± 14.2</td>
<td>85.6 ± 8.5</td>
</tr>
</tbody>
</table>

LES: lower oesophageal sphincter; HV: healthy volunteers. IQR: inter quartile range. Values are given in mean ± SEM. * p<0.05 compared to HV. No differences were seen between patients before and after ablation.
ablation (49 ± 7 mmHg, P = 0.03), but not compared to patients after ablation (58 ± 8 mmHg, P = 0.2).

No significant difference was found between healthy subjects and BE patients, nor between pre and post ablation measurements for the percentage normal peristalsis obtained after ten wet swallows (Table 2).

**Compliance measurement**

Compliance measurement of eight healthy volunteers and seven patients could be analysed. Due to technical problems, the data of two healthy subjects appeared to be incomplete, whereas in three patients the FLIP insertion failed (n = 1) or the patient refused to undergo the post-treatment procedure after completing the ablation protocol (n = 2).

**Figure 3.** Compliance of the oesophagogastric junction in 7 patients with early Barrett’s neoplasia before and after HALO ablation and in 8 healthy volunteers. Values are shown as mean with SEM.

Figure 3 shows the compliance of the distal esophagus as a plot of the cross-sectional area at the narrowest point through the EGJ plotted against bag pressure in healthy subjects and in BE patients before and after ablation. The compliance data was captured during the bag distension at 25 ml/min. In healthy volunteers, the mean compliance was 3.7 ± 0.9 mm²/cm H₂O. The compliance was significantly higher in patients than in healthy subjects (pre-ablation: 6.5 ± 0.9 mm²/cm H₂O; post-ablation: 7.3 ± 1.3 mm²/cmH₂O, P < 0.05). Compliance did, however, not change significantly in patients before and after ablation. Figure 3 also illustrates the mean threshold distension pressure required to achieve a CSA of 50 mm². This threshold pressure was substantially lower in BE patients compared to healthy volunteers. Furthermore, healthy subjects maintained a smaller CSA compared to BE patients, despite a larger increase in pressure during the distension.
Discussion

Endoscopic ablation therapy of early Barrett’s neoplasia aims to restore the normal squamous epithelium by controlled injury of the Barrett’s epithelium followed by subsequent healing under rigorous acid suppression therapy. If the depth of the injury is deeper than the muscularis mucosae, the treatment may damage the proper muscle layer which may cause subsequent scarring and retraction and ultimately affect the functional characteristics of the esophagus. In stepwise radical endoscopic resection, porfimer-PDT and high-power APC, damage to the proper muscle layer results in subsequent scarring and causes a symptomatic stenosis in up to 40% of patients treated.1-3, 17, 18

Stepwise circumferential and focal ablation using the HALO system is a relatively new endoscopic ablation technique, shown to successfully remove dysplastic and non-dysplastic BE.7, 8 A striking feature of this technique is the absence of ablation related stenosis. Studies in the porcine esophagus and in humans prior to a planned esophagectomy, have shown that HALO ablation results in complete epithelial ablation without submucosal injury or stricture formation.19, 20 Although the present study included only a relatively small number of patients, none of our patients developed a stenosis, which is in line with other clinical studies regarding this technique.8, 21, 22 However, the absence of the development of a stenosis does not exclude the possibility that more subtle changes contributing to impaired esophageal function and dysphagia are occurring as a result of ablation. Therefore, we evaluated the effect of ablative therapy on the compliance or distensibility of the distal esophagus, an indicator of resistance to stretch. To this end, we used the FLIP technique, a newly developed tool measuring multiple cross-sectional areas with concurrent pressure in a saline-filled bag during volume controlled distensions.9, 10, 15 Using this technique, we found no decrease in compliance of the distal esophagus after ablation. In addition, we determined the diameter of the distal esophagus prior to ablation and after complete regeneration of the Barrett’s segment to neosquamous mucosa, showing no decrease in esophageal diameter after ablation therapy. These results suggest that the elasticity or distensibility of the esophagus is well preserved, indirectly suggesting that no major change in wall structure has occurred. Alternatively, FLIP may not be sensitive enough to detect subtle changes. Previous studies however have demonstrated reduced compliance of the EGJ in achalasia patients 15, whereas we observed an increased compliance in GERD patients which is restored after a Nissen fundoplication (unpublished results). In line with these findings, the present study demonstrates an increased compliance in BE patients compared to healthy volunteers. Based on these findings, FLIP can be considered a reliable technique to detect changes in compliance. Other objective measurements of compliance or the diameter of the esophagus to evaluate the effect of other ablation techniques have not been performed yet.

Esophageal motility and LES function are important determinants of gastro-esophageal reflux. Therefore, endoscopic techniques developed to eliminate BE should preserve esophageal function, especially as contraction amplitude and LES pressure are already reduced in the majority of BE patients.23-26 Studies evaluating the effects of ablation therapy
on esophageal motility are however rather sparse.\textsuperscript{17, 18, 25, 27} One study showed a reduction in motility in some patients after photodynamic laser therapy \textsuperscript{18}, but most studies fail to demonstrate changes in esophageal motility after APC \textsuperscript{17}, multipolar electrocoagulation \textsuperscript{27} and porfimer-PDT.\textsuperscript{25} In the present study, we show that the HALO ablation technique also preserves the most important functional characteristics of the esophagus. Using manometry and esophageal sizing we found no reduction in LES-pressure, contraction amplitude or peristalsis. Contraction amplitude in the distal esophagus even increased and there was a slight increase in fully propagated contraction waves after ablation. Taken together, these data demonstrate that RFA using the HALO system preserves esophageal motility.

In addition to motility, recent insights clearly indicate that compliance or distensibility of the esophagogastric junction largely determines the probability for reflux to occur. For example, Pandolfino \textit{et al.} demonstrated that the compliance of the esophagus is increased in GERD patients, contributing to an increased risk to have liquid reflux during sphincter opening.\textsuperscript{28} In line with this, Nissen fundoplication yields its antireflux effect by restoring EGJ compliance.\textsuperscript{29, 30} These data indicate that distensibility of the distal esophagus provides important additional information on EGJ and esophageal competence. In concordance with the above mentioned studies, we found an increased compliance in BE patients compared to HV. Together with the decreased LES length and LES resting pressure, this increased compliance most likely plays an important role in the increased rate of gastro-esophageal reflux in BE patients. One should consider though that the difference in age between the groups in our study most likely exaggerates the observed differences in compliance and LES function between HV and BE patients.

A possible shortcoming of our study is that we could only measure compliance over a segment length of 3.5 cm, indicating that the probe did not cover the entire treated segment. The FLIP technique might thus benefit by increasing the number of CSAs that can be measured. Optimizing the technique and increasing the number of patients and patients groups are needed to confirm the usefulness of FLIP in defining changes in compliance before and after endoscopic treatments.

In summary, when compared to healthy subjects, BE patients have an impaired esophageal function with a decreased LES length and LES pressure, a decreased contraction amplitude, and an increased EGJ compliance. Radiofrequency ablation was found to have no further adverse effect on these parameters and appears to be the first ablation technique to achieve the right trade-off between effectiveness on one hand and the avoidance of damage to the deeper layers on the other hand, thus preserving the functional integrity of the treated distal esophagus.

\section*{Reference List}


Chapter 3


