Douglas G. Adler MD, FACG, AGAF, FASGE, Series Editor

Endoscopic Management of Barrett's Esophagus: An Update on Radiofrequency Ablation

Amaninder S. Dhaliwal

Benjamin Tharian

Mohit Girotra

BACKGROUND

Barrett's esophagus (BE), first described in 1950 by Dr. Norman Barrett, a British thoracic surgeon, refers to replacement of normal squamous epithelium of the esophagus by columnar epithelium, at least 1cm above the gastro-esophageal junction (GEJ).[1] It is considered a precursor lesion of esophageal adenocarcinoma (EAC). The incidence of BE is increasing in the western world has paralleled the increase in endoscopic procedures worldwide. The risk of EAC in patients with BE, which was earlier projected to be significantly higher, is now estimated at least 10 fold higher when compared to the general population.[2] The reason for this decline in risk as compared to the previous studies may be due to the earlier recognition of dysplastic changes and improved endoscopic ablative therapies.[3] In the United States, the overall mortality with EAC is high, and 5-year survival rate is under 20% per SEER cancer statistics review (1975-2011). Since transformation of BE into EAC involves progression of dysplasia, surveillance is important at an early stage, for the reduction in the overall mortality in EAC.[3]

Risk Factors for BE

Gastro-esophageal reflux disease (GERD) is considered an independent risk factor for BE and has been on a rise in the western world with a prevalence of 10-20%.[5]

Amaninder S. Dhaliwal, MBBS, Resident in Internal Medicine, Department of Medicine, NYU School of Medicine/Brooklyn Campus, NY, Benjamin Tharian, MD, MRCP (Med, Gastro), FRACP, Assistant Professor, Division of Gastroenterology and Hepatology, Department of Medicine, University of Arkansas for Medical Sciences (UAMS), Little Rock, AR, Mohit Girotra, MD, FACP, Assistant Professor, Division of Gastroenterology and Hepatology, Department of Medicine, University of Arkansas for Medical Sciences (UAMS), Little Rock, AR

Acknowledgements

The authors are grateful to Dr. Lauren G. Khanna (Assistant Professor, Division of Gastroenterology, NYU Langone Medical Center, New York) and Dr. Farshad Aduli (Former Associate Professor, University of Arkansas for Medical Sciences, Little Rock, AR) for allowing us to utilize Barrett's and RFA pictures from their patients. We also thank Mr. Jared Pittman from Medtronic, for providing us the consolidated image of all available RFA catheters.

About 15% patients with chronic GERD can develop BE, as compared to 1-2% of general population.[6] Males are more predisposed to develop BE/EAC than females with ratio of 2:1. Caucasian males over the age of 60 years with chronic GERD symptoms are at higher risk for developing BE/EAC than males under the age of 50 years or women.[7]

While cigarette smoking is strongly associated with both BE and GERD,[8,9] the relationship of alcohol consumption and BE is conflicting.[10] Classically, alcohol has been considered as a risk factor, especially in combination with smoking. A recent study proposed that wine consumption was associated with reduced risk of BE, although no consistent dose-response relationship could be established for this protective effect.[10] Central obesity is another significant risk factor for BE, independent of overall body fat (measured by body mass index, BMI), in both men and women.[11] Metabolic syndrome, obstructive sleep apnea, and some germ-line mutations have also been implicated as additional risk factors for BE.

Diagnosis of BE

BE is traditionally classified based on endoscopic length of salmon colored mucosa, as long segment (LSBE > 3cm) or short segment (SSBE < 3 cm).[12] However, diagnosis of BE needs histological correlation in addition to endoscopic appearance, which takes into account replacement of esophageal squamous epithelium by columnar epithelium (CE) along with presence of goblet cells, a marker of intestinal metaplasia (IM).[15,16] The significance of these two histological features can be appraised by considering the debate around insufficient diagnosis of BE in presence of CE in distal esophagus (1cm above GEJ) but without IM.[13] Moreover, epidemiological evidence suggests that patients with CE without IM are at low risk of developing EAC as compared to patients with CE and IM (0.07% vs 0.38%.[14] Hence, the current American College of Gastroenterology (ACG) clinical guideline recommends obtaining at least 8 biopsies in patients with suspected BE < 2cm and four quadrant 2-cm biopsies in segments > 2cm, whereas it recommends against endoscopic biopsy of normal or irregular Z-line of less than 1 cm from GEJ.[15,18]

In cases of suspected BE, documentation of endoscopic landmarks (GEJ, diaphragmatic hiatus: DH) along with measurement of maximal (M) and circumferential (C) length of visible segment of

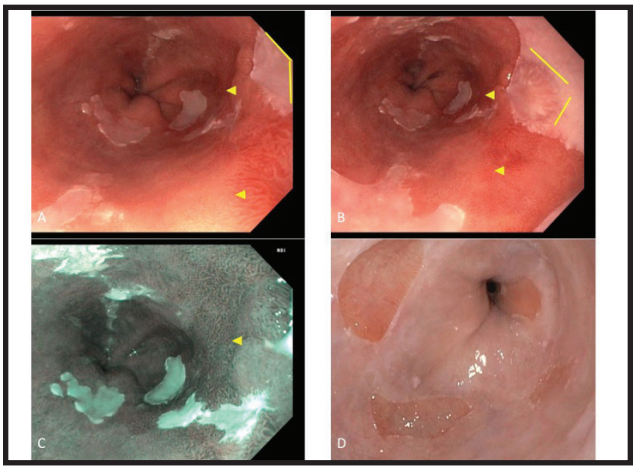

Figure 1. A. Salmon colored mucosa visualized under white-light endoscopy (WLE) B. The yellow lines mark the top of circumferential portion (C) and maximal extent (M) thus representing Prague classification C. Same segment visualized under narrow band imaging (NBI) D. Isolated islands of salmon colored mucosa.

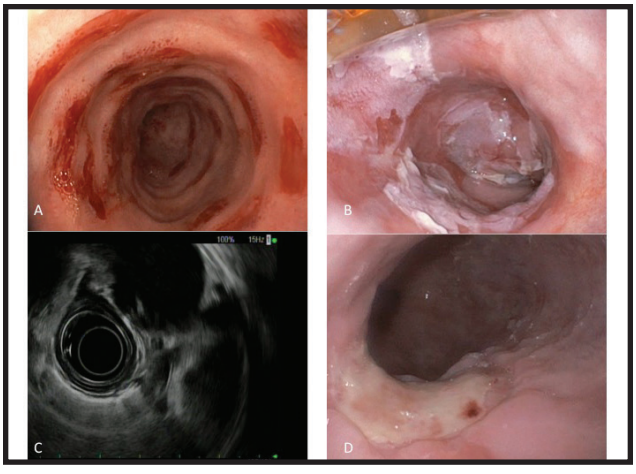

Figure 2. A. Seattle protocol of BE biopsies (random 4-quadrant biopsies every 1 cm versus 2 cm in patients with and without prior history of dysplasia respectively) B. RFA 90 ablation of dysplastic BE; C: Use of Endoscopic ultrasound (EUS) to view the layers of esophagus, to confirm absence of mass or lymph nodes D. Post-RFA ulcer.

BE should be mandatorily performed using the Prague classification (Figure 1). Sharma et al. have demonstrated that reliability coefficient (RC) for endoscopic landmarks (GEJ: RC 0.88; DH: RC 0.85) and of BE segment >1 cm (RC 0.72) is high when Prague classification is used.[17]

Screening Methods for BE

Currently, screening for BE is limited to patients with recognized high-risk factors like chronic GERD,

caucasian race, male gender, age > 60 years, smoking, central obesity and confirmed family history of BE, but not extended to the general population. While this can be achieved using various techniques like conventional endoscopy (CEGD), unsedated transnasal endoscopy (TNE), esophageal video capsule endoscopy (VCE) and cytosponge, CEGD remains the gold standard because of its ability to achieve histological correlation. While limited evidence may support TNE for its comparable efficacy to CEGD (sensitivity and specificity 91% and 100% respectively) for diagnosing BE, especially given its ease of performance with minimal complications,[19] it still needs multi-centric validation. VCE appeals as a non-invasive screening method, but should be reserved for patients who refuse CEGD, given its lower sensitivity and specificity (78% and 73% respectively), no cost advantage and inability of histological sampling.[20] Contrarily, cytosponge is an emerging non-invasive yet cost effective screening tool, which if followed by dysplasia and intra-mucosal cancer treatment, may reduce the incidence of symptomatic EAC in high-risk patients by 19%.[21]

High-definition white light endoscopy (HD-WLE) is superior for both screening and surveillance of BE, over standard-definition endoscopy, for detecting dysplastic lesions.[22] Since standard protocol biopsies have high miss rate of dysplasia, advance imaging, including chromoendoscopy, narrow band imaging (NBI) and confocal laser endomicroscopy (CLE), are increasingly being employed to further increase the rate of detection of dysplastic lesions as well as EAC. Chromoendoscopy utilizes a special dye (methylene blue, acetic acid or indigo carmine) to enhance the dysplastic lesions, which helps in better visualization during the endoscopy. NBI also referred to as virtual chromoendoscopy, works on the same principle as above, except that it utilizes narrow band filters instead of spraying dyes.[23] Sharma et al. compared NBI to HD-WLE using Seattle protocol and found that fewer biopsies were required using NBI when compared to HD-WLE, with similar overall IM detection rates.[24] Although NBI is considered superior to HD-WLE, it's yield of detecting early neoplasia is controversial, but is still being suggested as the diagnostic modality of choice for surveillance in BE.[23] CLE magnifies the mucosal patterns of dysplastic lesions by thousand folds enabling to visualize them to the cellular level.[25] However, its use is limited as evidence from the prospective studies suggests that CLE does not help in increasing the overall detection rates of IM.[25] Increased time to examine during endoscopy is associated with higher detection rates of dysplasia and EAC.[26]

Management of BE

The strong argument for endoscopic eradication of BE rather than a permissive surveillance approach arises from several facts, as elucidated. BE is a precancerous state with a "field defect", and is the first step in the "metaplasia-dysplasia-cancer" sequence, in which molecular aberrations precede neoplasia and radiofrequency ablation (RFA) can eliminate such mutations.[27,28] Furthermore, a multicenter study found that over 50% of those who developed high-grade dysplasia (HGD) or cancer while undergoing surveillance did not have prior findings of dysplasia, suggesting that the "wait and watch" policy might be inadequate to reliably detect early changes.[29,30]

The incidence of EAC in the general population (0.003%) goes up by 200 (0.6%), 560 (1.7%) and 2,200 (6.6%) folds once an individual develops BE, low-grade dysplasia (LGD) and HGD respectively,[31] per SEER cancer statistics review (1975-2011). This is in sharp contrast to the incidence of colon cancer (0.048%), which increases 12 folds (0.58%) with development of a polyp.[32] Like colonic polyps are actively managed with polypectomy followed by surveillance, experts endorse similar philosophy in BE management, to steer the paradigm from surveillance only to dysplasia treatment followed by surveillance.[33] It is noteworthy that less than 50% endoscopists adhere to the Seattle Protocol for BE biopsies. Even if adherence is sustained, it still leaves behind a large unsampled segment of esophagus. Lastly, there still remains a high interobserver variation between pathologists, especially in the diagnosis of indefinite or indeterminate dysplasia (ID) and low-grade dysplasia (LGD). All these facts must be deliberated to maintain a perspective during management of BE.

The treatment modalities for BE can be categorized as endoscopic, surgical and chemoprophylaxis.

Endoscopic Management

Per Seattle protocol, targeted biopsies of suspicious dysplastic lesions should be performed along with random 4-quadrant biopsies every 1 cm versus every 2 cm in patients with and without prior history of dysplasia respectively.[34] (Figure 2). Subsequent management depends on whether the BE is smooth or nodular. Most of the ablation treatments like RFA and cryotherapy

are effective only on a smooth non-nodular esophagus. Hence any nodularity or mucosal / vascular abnormality visualized on endoscopy should be managed by endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD) for histopathological staging of the lesion (Figure 3). A study on 293 consecutive endoscopic resections demonstrated that use of EMR alone changed the diagnosis and treatment policy in 49% and 30% of the lesions respectively.[35] The subsequent management after EMR depends upon the histological staging of the endoscopic resections.

Patients with non-dysplastic BE (NDBE) should be engaged in endoscopic surveillance every 3-5 years and do not need endoscopic ablative techniques (EAT), given the low incidence of dysplasia and EAC in this population. Recent data estimates that 98.6% and 97.1% NDBE patients remain cancer free after 5-year and 10-year follow-up respectively.[36] On the other hand, presence of indefinite/indeterminate dysplasia (ID) is a trickier situation, and such patients should undergo repeat endoscopic evaluation after aggressive PPI treatment in 3-6 months. It is now proposed that patients with ID may carry a significant risk of harboring prevalent dysplasia, although the risk of incident dysplasia is similar to the general BE population.[37] Hence, ACG guideline suggests surveillance for these patients like those with LGD, especially because the risk of progression to cancer or dysplasia (LGD/HGD) is highest during the first year. Skacel et al. showed that LGD progressed to HGD over a median of 11 months, in 41% and 80% respectively, depending on whether two or three independent pathologists concurred with the initial diagnosis of LGD.[38]

The confirmed cases of BE with LGD (BE-LGD) should be reviewed by a second pathologist for adequate staging of dysplasia and risk stratification[39] followed by aggressive acid suppression aimed at downgrading the dysplasia. If dysplasia resolves, these patients can be surveyed annually for 2 years after which this interval may be increased. If LGD persists, the current ACG guideline endorses endoscopic treatment, although acknowledges yearly endoscopic surveillance as an acceptable alternative. However, there is emerging data favoring endoscopic therapy over surveillance by demonstrating decreased risk of neoplastic progression after 3 years.[40] Similarly, patients with HGD require histological confirmation by a second expert pathologist, concomitant acid suppression, but are candidates for endoscopic interventions. Currently, EAT is preferred

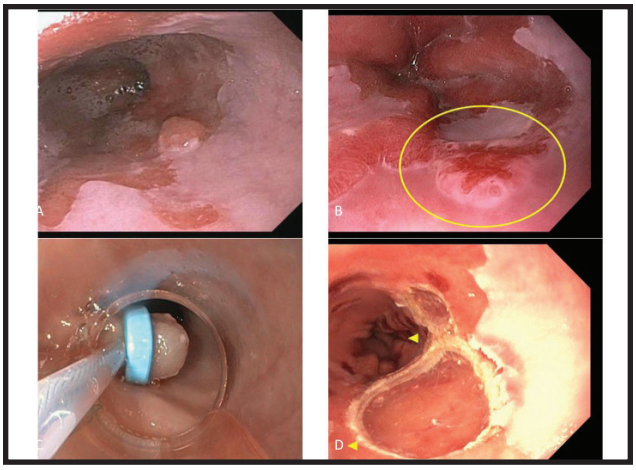

Figure 3. A and B. Spectrum of nodules/lumps seen in BE patients, raising concerns for early adenocarcinoma (EAC) C. Ligation assisted EMR of a nodule D. Post EMR view of submucosa.

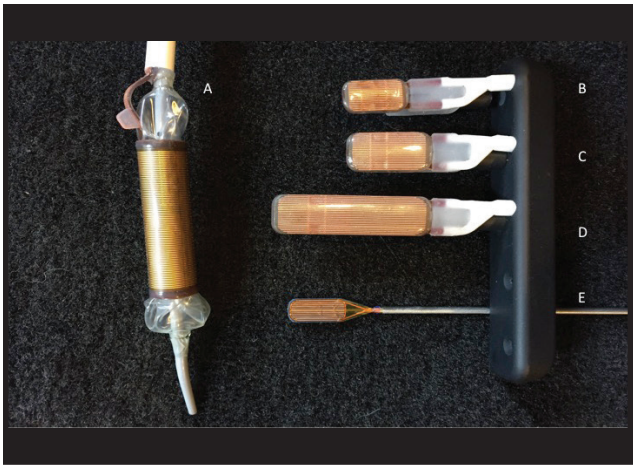

Figure 4. Available BARRYXTM Ablation Catheters for RFA. A. RFA 360 (Diameter range 18-31mm): Two types – Express catheter with balloon length 8cm and electrode length 4cm (sizing balloon not needed) and Standard catheter with balloon length 6cm and electrode length 3 cm (requires sizing balloon) B. RFA 60 (Electrode 15 x 10mm) C. RFA 90 (Electrode 20 x 13mm) D. RFA Ultralong (Electrode 40 x 13mm) E. Channel RFA (Electrode 15.7 x 7.5mm) Courtesy: Jared Pittman, Interventional Account Manager, Medtronic (with permission)

over esophagectomy as the treatment choice for patients with BE-HGD for its proven efficacy, cost effectiveness and better adverse event profile.[41]

EAC is staged depending upon the depth of invasion as T1a (limited to mucosa), T1b sm1 (extension into upper one-third of submucosa), T1b sm2 (extension into middle one-third of submucosa) and T1b sm3 (extension into deep one-third of submucosa). The risk of lymph node (LN) metastases in patients with

(continued on page 34)

(continued from page 32)

BE-HGD and IMC is estimated at 0% and <2% respectively,[42] hence EAT makes sense as the preferred treatment strategy. However, situation gets murkier with EAC. Surgical literature estimates up to 7% and 27% LN metastases risk in patients with EAC T1a and T1b respectively43, therefore making this distinction of paramount importance. However, data on accuracy of EUS for staging of superficial esophageal cancers (T1a, T1b sm1) is limited, and hence EMR remains the gold standard.[44-46]

EAT remains the treatment of choice for BE patients with dysplasia, T1a EAC and well-differentiated T1b sm1 EAC with no lympho-vascular spread.[47] The various EAT include radiofrequency ablation (RFA), photodynamic therapy (PDT) and cryotherapy. For limited surface areas, argon plasma coagulation and bipolar probes are a less expensive alternative, although they may have higher recurrence rates, and hence rarely preferred. RFA is the preferred modality for most patients as it is cost effective and has better adverse event profile than PDT or cryotherapy, and would be the main focus of discussion in this article.

Surgical Management

Endoscopic therapy for HGD/IMC has similar survival (94% at 3 years both groups) but lower morbidity (0% vs. 39%; P<0.0001) compared to esophagectomy.[48] Esophagectomy in combination with chemo-radiation is the treatment of choice for patients with advanced EAC (T1b sm2-3) or high-risk superficial EAC (poor differentiation or lymphovascular invasion).[49] While robust acid suppression is an accepted strategy to decrease neoplastic progression of BE, anti-reflux surgeries have no proven efficacy and hence not recommended.[50] The SAGES guideline also endorses endoscopic treatment modalities.[51] Reflux surgery should be considered in individuals with objective evidence of reflux that fails to respond to PPI, especially those with hiatus hernia, before, during or after ablation treatment.

Chemoprophylaxis

In addition to symptomatic control of GERD, PPIs also serve an additional role as chemoprophylactic agents, given their effect on decrease dysplasia/EAC in patients with BE.[52] Additionally, data exists describing beneficial effects of NSAID'S, aspirin and statins in reducing incidence of EAC in BE patients, but none are currently endorsed exclusively for their anti-neoplastic effects.[53-54]

An Update on Radiofrequency Ablation (RFA)

a. Types of RFA catheters and Biophysiology

RFA combined with EMR has become the standard treatment for BE because of increased efficacy, cost effectiveness and better side effect profile. The biophysical principle of RFA ablation therapy is using electricity in the radiofrequency range of 450-500 kHz for small vessel and tissue destruction.[55] Barrett's epithelium is approximately 500 µm thick, and RFA is designed to achieve a uniform, superficial depth of ablation between ~ 500 µm and ~ 1,000 µm in short bursts of ~ 1 sec, thus achieving optimal removal of esophageal epithelium with minimal risk for complications like buried glands or stricture formation. The ablative energy ranges between 12J/cm2 to 15J/cm2; the use of N-acetyl cysteine sprayed over esophageal mucosa is encouraged for effective contact between RFA catheter and the mucosa.[56] There are different RFA catheters available for circumferential and focal therapies, as depicted in Figure 4. (BarrxTM ablation system, Covidien-Medtronic, Sunnyvale, CA). The Barrx360 3cm catheter is used for ablation of circumferential dysplastic mucosa, whereas Barrx90 focal/ultra-long, Barrx60 and channel catheters are employed for focal ablation of small isolated areas/islands of dysplasia and possibly for short segment BE. Smaller and channel catheters have added advantage of being useful in patients with difficult anatomy and strictures.[57]

b. Efficacy and Safety of RFA

In a sham-controlled trial performed on patients with dysplastic BE, RFA was associated with a high rate of complete eradication of both dysplasia (CED = 90.5% vs. 22.7%; p<0.001) and intestinal metaplasia (CEIM = 77.4% vs. 2.3%; p<0.001) and a reduced risk of disease progression (3.6% versus 16.3%; p=0.03).[58] at 12 months. A subsequent multi-centric study reported eradication of dysplasia and CEIM in 98% and 91% patients respectively, thus establishing durability of this therapy.[59] In addition to the proven role of RFA in BE with dysplasia, its utility in patients with NDBE is often discussed. In a multi-centric trial from 8 centers in the US, Fleischer et al. reported 98% complete eradication of intestinal metaplasia (CEIM) in NDBE patients with

Table 1. Up-to-Date Studies on RFA

Study and Year	Type of Intervention	Median BE length (cm)	No. of patients (N)	Mean Age (years)	Type of Dysplasia	Length of Follow-up (months)	CED (%)	CEIM (%)
Fleischer 2008[50]	C-RFA followed by FA	6	62	55.5	NDBE	30	-	98
Ganz 2008[75]	C-RFA	6	142	66	NDBE, HGD, LGD	12	80.4	54.3
Shaheen 2009[48]	C-RFA followed by FA	4.6	42	33	LGD	12	90	81
		5.3	42	37	HGD	12	81	74
Sharma 2009[76]	C-RFA followed by FA	5	63	57	LGD, HGD	24	89	79
Velanovich 2009[77]	C-RFA followed by FA	3	66	53	NDBE, HGD, LGD	12	93	-
Lyday 2010[78]	C-RFA followed by FA	3	137	97	NDBE, HGD, LGD	20	100	77
Fleischer 2010[58]	C-RFA followed by FA	3.1	50	54.3	NDBE	60	-	92
Pouw 2010[79]	C-RFA followed by FA+EMR	8	24	65	HGD, IMC	22	100	96
Shaheen 2011[49]	C-RFA followed by FA	4.5	58	65.5	LGD	24	98	98
		5.2	61	66.4	HGD	24	93	89
Bergman 2011[80]	C-RFA followed by FA	6.2	29	60.3	LGD, HGD, IMC	12	97	-
Zemlyak 2012[81]	C-RFA followed by FA	>Or <2cm	70	61	NDBE.LGD, HGD	16.1	81*	-
Bulsiewicz 2013[82]	C-RFA followed by FA+EMR	4	210	64.4	LGD, HGD, IMC	>12	87	80
Haidry 2013[46]	C-RFA followed by FA+EMR	5.8	335	69	LGD, HGD, IMC	12	81	62
Phoa 2013[83]	C-RFA followed by FA+EMR	5	55	65	LGD, HGD, IMC	60	90	90
Pasricha 2014[84]	C-RFA followed by FA+EMR	4	1634	61.7	NDBE, HGD, LGD, EAC	28	80	-
Haidry 2015[54] 2011-2013	C-RFA followed by FA+EMR	4.7	242	69	LGD, HGD, IMC	10	92	83
2008-2010		6	266	68	LGD, HGD, IMC	12	77	57
He 2015[85]	C-RFA followed by FA	8.6	96	59.9	LGD, HGD, EAC	12	84*	-

Abbreviations: C-RFA: Circumferential Radiofrequency Ablation; FA: Focal Ablation; EMR: Endoscopic Mucosal Resection; BE: Barrett's Esophagus; ID: Indefinite Dysplasia; LGD: Low Grade Dysplasia; HGD: High Grade Dysplasia; IMC: Intra-mucosal Carcinoma; EAC: Esophageal Adenocarcinoma; CED: Complete Eradication of Dysplasia; CEIM: Complete Eradication of Intestinal Metaplasia

*Studies by Zemlyak and He only reported results as complete response (not as CED and CEIM)

ablative therapies over 2.5 years follow-up.[60] The same authors later obtained biopsies from previous known length of BE at 5 years to demonstrate 92% (46/50) CEIM and the remaining 8% had easy conversion to CEIM with single session of focal RFA.[61] Although RFA is efficacious and durable in NDBE patients, however, given the low risk of its progression to cancer, the current ACG guideline recommends against routine application of endoscopic therapies in these patients.

Although these studies established RFA as the cornerstone treatment for dysplastic BE, our understanding regarding indications is still evolving and we are constantly striving to improve in this area. The major RFA studies have been tabulated in Table 1. We also know that RFA is associated with improved quality of life (QoL) in dysplastic BE. Ablation alters the natural history of BE.[62] Wani et al. in their meta analysis showed that the progression risk to cancer went down to 0.16%, 0.16% and 1.7% for NDBE, LGD and HGD respectively with ablation, with the number needed to treat (to avoid one cancer over 5 years) being 45, 13 and 4 respectively.[31] Das et al. concluded from his economic analysis study that radiofrequency ablation was more cost-effective than surveillance even for non-dysplastic BE.[63]

c. Efficacy of RFA+EMR over RFA

In patients with dysplastic BE (both HGD and LGD), EMR+RFA is superior to RFA alone, based on higher efficacy (18% vs. 10%).[64] Also, EMR prior to RFA was found to be as safe in patients with BE/EAC as was RFA alone with no higher stricture formation rates.[65] Furthermore, a comparison of outcomes in BE patients between 2011-2013 and 2008-2010 from the UK demonstrated significantly higher CEIM (83% vs. 56%) and CED (92% vs. 77%) in recent time period, most of which was attributable to improved lesion recognition and aggressive resection of visible lesions prior to RFA (with EMR), though progression to EAC was not statistically different (2.1% vs 3.4%)66. Most importantly, EMR provides the most accurate staging, and helps plan further management of patients with BE/EAC.

Extensive EMR alone may be an alternative strategy for management of dysplastic BE. However, a multicenter trial established that in patients with ≤ 5cm segment BE/HGD, stepwise radical EMR (SEMR) and RFA+EMR achieved high rates of CED (100% vs. 96%), but SEMR group had more stenosis (88% vs. 14%; $p<0.001$) requiring subsequent endoscopic treatments.[67]

Hence, EMR+RFA is now recognized to be efficacious, safe and superior to RFA or EMR alone, in management of dysplastic BE.

d. Association of Acid Control and RFA Outcomes

Concurrent anti-reflux therapy is an important concept in patients with BE, especially in those who undergo therapy. A retrospective study of RFA outcomes in patients with BE suggested better CEIM rates in BE patients with normal-mild esophageal acid exposure as compared to patients with moderate-severe acid exposure (44% vs. 15%),[68] thus endorsing effective intra-esophageal pH control for improved RFA outcomes.[68,69] Moreover, inadequate control of reflux post ablation may result in recurrence.[69,70] The ACG endorses use of PPI in daily doses in BE patients, unless warranted in twice-daily doses because of reflux symptoms or esophagitis.[15] Although not a recommendation, most experts use PPI in twice daily dose after RFA to minimize complications, especially stricture formation.

e. Recurrence of IM after RFA

In a recent retrospective cohort of patients with BE and dysplasia/IMC who achieved CEIM, the post-RFA recurrence rates for IM and EAC progression were ascertained to be 5.2%/year and 1.9%/year respectively.[71] Subsequently using the much larger US RFA registry, it was demonstrated that after CEIM, BE recurrence may occur in upto 20% patients, and is usually very short (0.6 cm average length) and non-dysplastic/indefinite for dysplasia in 86%.[72] The study identified older age, non-Caucasian race, increasing length of BE length and advanced pre-treatment histology as risk factors for recurrence, and these are now taken into account while planning post-RFA surveillance intervals.[73] Subsequent studies revealed area around GEJ as most vulnerable for IM recurrence.[74]

Since no specific characteristics are currently established which accurately predict recurrence, it is important for subjects undergoing RFA for dysplastic BE to be retained in endoscopic surveillance programs. Modalities like laser assisted Optical coherence tomography (OCT) and Confocal laser endomicroscopy (CLE) have been used to assist the endoscopist in the post RFA surveillance phase to pick up "buried glands" and early recurrence, and to target treatment.

(continued on page 38)

(continued from page 36)

CONCLUSIONS

In summary, while cryotherapy and PDT are available alternatives, RFA in conjunction with EMR is the most robustly studied and practiced endoscopic technique for management of dysplastic BE, with high success, cost effectiveness and very few limitations. The modality and equipment are a work-in-evolution, and have plenty of areas requiring continued research. However, the bottom line remains that endoscopists should carefully inspect the Barrett's mucosa, both pre and post ablation as part of surveillance. We endorse that the modality of choice for endoscopic eradication of Barrett's esophagus must be in accordance with endoscopist's training and preference, institutional availability and patient characteristics. ■

References

1. Jung, K. W., Talley, N.J., Romero, Y., Katzka, D.A., Schleck, C.D., Zinsmeister, A.R. et al. Epidemiology and natural history of intestinal metaplasia of the gastroesophageal junction and Barrett's esophagus: a population-based study. Am J Gastroenterol 106, 1447-1455; quiz 1456, doi:10.1038/ajg.2011.130 (2011).
2. Hvid-Jensen, F., Pedersen, L., Drewes, A. M., Sorensen, H. T. & Funch-Jensen, P. Incidence of adenocarcinoma among patients with Barrett's esophagus. N Engl J Med 365, 1375-1383, doi:10.1056/NEJMoa1103042 (2011).
3. Thrift, A. P. The epidemic of oesophageal carcinoma: Where are we now? Cancer Epidemiol 41, 88-95, doi:10.1016/j.canep.2016.01.013 (2016).
4. van Sandick, J. W., Van Lanschot, J.J., Kulken, B.W., Tytgat, G.N., Offerhaus, G.J., Obertop, H. et al. Impact of endoscopic biopsy surveillance of Barrett's oesophagus on pathological stage and clinical outcome of Barrett's carcinoma. Gut 43, 216-222 (1998).
5. El-Serag, H. B., Sweet, S., Winchester, C. C. & Dent, J. Update on the epidemiology of gastro-oesophageal reflux disease: a systematic review. Gut 63, 871-880, doi:10.1136/gutjnl-2012-304269 (2014).
6. Ronkainen, J. Aro, P., Storskrubb, T., Johansson, S.E., Lind, T, Bolling-Sternevald, E. et al. Prevalence of Barrett's esophagus in the general population: an endoscopic study. Gastroenterology 129, 1825-1831, doi:10.1053/j.gastro.2005.08.053 (2005).
7. Rubenstein, J. H., Scheiman, J. M., Sadeghi, S., Whiteman, D. & Inadomi, J. M. Esophageal adenocarcinoma incidence in individuals with gastroesophageal reflux: synthesis and estimates from population studies. Am J Gastroenterol 106, 254-260, doi:10.1038/ajg.2010.470 (2011).
8. Andrici, J., Cox, M. R. & Eslick, G. D. Cigarette smoking and the risk of Barrett's esophagus: a systematic review and meta-analysis. J Gastroenterol Hepatol 28, 1258-1273, doi:10.1111/jgh.12230 (2013).
9. Cook, M. B., Shaheen, N.J., Anderson, L.A., Giffen, C., Chow, W.H., Vaughan, T.L. et al. Cigarette smoking increases risk of Barrett's esophagus: an analysis of the Barrett's and Esophageal Adenocarcinoma Consortium. Gastroenterology 142, 744-753, doi:10.1053/j.gastro.2011.12.049 (2012).
10. Thrift, A. P., Cook, M.B., Vaughan, T.L., Anderson, L.A, Murray, l.J., Whiteman, D.C. et al. Alcohol and the risk of Barrett's esophagus: a pooled analysis from the International BEACON Consortium. Am J Gastroenterol 109, 1586-1594, doi:10.1038/ajg.2014.206 (2014).
11. Kubo, A., Cook, M.B., Shaheen, N.J., Vaughan, T.L., Whiteman, D.C., Murray, L., et al. Sex-specific associations between body mass index, waist circumference and the risk of Barrett's oesophagus: a pooled analysis from the international BEACON consortium. Gut 62, 1684-1691, doi:10.1136/gutjnl-2012-303753 (2013).
12. Sharma, P., Morales, T. G. & Sampliner, R. E. Short segment Barrett's esophagus--the need for standardization of the definition and of endoscopic criteria. Am J Gastroenterol 93, 1033-1036, doi:10.1111/j.1572-0241.1998.00324.x (1998).
13. Fitzgerald, R. C., di Pietro, M., Ragunath, K., Ang, Y., Kang, J.Y., Watson, P. et al. British Society of Gastroenterology guidelines on the diagnosis and management of Barrett's oesophagus. Gut 63, 7-42, doi:10.1136/gutjnl-2013-305372 (2014).
14. Bhat, S., Coleman, H.G., Yousef, F., Johnston, B.T., McManus, D.T., Gavin, A.T. et al. Risk of malignant progression in Barrett's esophagus patients: results from a large population-based study. J Natl Cancer Inst 103, 1049-1057, doi:10.1093/jnci/djr203 (2011).
15. Shaheen, N. J., Falk, G. W., Iyer, P. G. & Gerson, L. B. ACG Clinical Guideline: Diagnosis and Management of Barrett's Esophagus. Am J Gastroenterol 111, 30-50, doi:10.1038/ajg.2015.322 (2016).
16. Khandwalla, H. E., Graham, D.Y., Kramer, J.R., Ramsey, D.J., Duong, N., Green, L.K. et al. Barrett's esophagus suspected at endoscopy but no specialized intestinal metaplasia on biopsy, what's next? Am J Gastroenterol 109, 178-182, doi:10.1038/ajg.2013.408 (2014).
17. Sharma, P., Dent, J., Armstrong, D., Bergman, J.J., Gossner, L., Hoshihara, Y. et al. The development and validation of an endoscopic grading system for Barrett's esophagus: the Prague C & M criteria. Gastroenterology 131, 1392-1399, doi:10.1053/j.gastro.2006.08.032 (2006).
18. Harrison, R., Perry, I., Haddadin, W., McDonald, S., Bryan, R., Abrams, K. et al. Detection of intestinal metaplasia in Barrett's esophagus: an observational comparator study suggests the need for a minimum of eight biopsies. Am J Gastroenterol 102, 1154-1161, doi:10.1111/j.1572-0241.2007.01230.x (2007).
19. Shariff, M. K., Bird-Lieberman, E.L., O'Donovan, M., Abdullahi, Z., Liu, X., Blazeby, J. et al. Randomized crossover study comparing efficacy of transnasal endoscopy with that of standard endoscopy to detect Barrett's esophagus. Gastrointest Endosc 75, 954-961, doi:10.1016/j.gie.2012.01.029 (2012).
20. Bhardwaj, A., Hollenbeak, C. S., Pooran, N. & Mathew, A. A meta-analysis of the diagnostic accuracy of esophageal capsule endoscopy for Barrett's esophagus in patients with gastroesophageal reflux disease. Am J Gastroenterol 104, 1533-1539, doi:10.1038/ajg.2009.86 (2009).
21. Benaglia, T., Sharples, L. D., Fitzgerald, R. C. & Lyratzopoulos, G. Health benefits and cost effectiveness of endoscopic and nonendoscopic cytosponge screening for Barrett's esophagus. Gastroenterology 144, 62-73 e66, doi:10.1053/j.gastro.2012.09.060 (2013).
22. Sami, S. S., Subramanian, V., Butt, W.M., Bejkar, G., Coleman, J., Mannath, J. et al. High definition versus standard definition white light endoscopy for detecting dysplasia in patients with Barrett's esophagus. Diseases of the esophagus : official journal of the International Society for Diseases of the Esophagus / I.S.D.E 28, 742-749, doi:10.1111/dote.12283 (2015).
23. Qumseya, B. J., Wang, H., Badie, N., Uzomba, R.N., Parasa, S., White, D.L. et al. Advanced imaging technologies increase detection of dysplasia and neoplasia in patients with Barrett's esophagus: a meta-analysis and systematic review. Clin Gastroenterol Hepatol 11, 1562-1570 e1561-1562, doi:10.1016/j.cgh.2013.06.017 (2013).
24. Sharma, P., Hawes, R.H., Bansal, A., Gupta, N., Curvers, W., Rastogi, A. et al. Standard endoscopy with random biopsies versus narrow band imaging targeted biopsies in Barrett's oesophagus: a prospective, international, randomised controlled trial. Gut 62, 15-21, doi:10.1136/gutjnl-2011-300962 (2013).
25. Wang, K. K., Okoro, N., Prasad, G., WongKeeSong, M., Buttar,

N.S., Tian, J. Endoscopic evaluation and advanced imaging of Barrett's esophagus. Gastrointest Endosc Clin N Am 21, 39-51, doi:10.1016/j.giec.2010.09.013 (2011).
26. Gupta, N., Gaddam, S., Wani, S.B., Bansal, A., Rastogi, A., Sharma, P. Longer inspection time is associated with increased detection of high-grade dysplasia and esophageal adenocarcinoma in Barrett's esophagus. Gastrointest Endosc 76, 531-538, doi:10.1016/j.gie.2012.04.470 (2012).
27. Fleischer, D. E., Odze, R., Overholt, B.F., Carroll, J., Chang, K.J., Das, A. et al. The case for endoscopic treatment of non-dysplastic and low-grade dysplastic Barrett's esophagus. Dig Dis Sci 55, 1918-1931, doi:10.1007/s10620-010-1218-1 (2010).
28. Pouw, R. E., Gondrie, J.J., Rygiel, A.M., Sondermeijer, C.M., Ten Kate, F.J., Odze, R.D. et al. Properties of the neosquamous epithelium after radiofrequency ablation of Barrett's esophagus containing neoplasia. Am J Gastroenterol 104, 1366-1373, doi:10.1038/ajg.2009.88 (2009).
29. Falk, G. W., Ours, T. M. & Richter, J. E. Practice patterns for surveillance of Barrett's esophagus in the united states. Gastrointest Endosc 52, 197-203, doi:10.1067/mge.2000.107728 (2000).
30. Sharma, P., Falk, G.W., Weston, A.P., Reker, D., Johnston, M., Sampliner, R.E. Dysplasia and cancer in a large multicenter cohort of patients with Barrett's esophagus. Clin Gastroenterol Hepatol 4, 566-572, doi:10.1016/j.cgh.2006.03.001 (2006).
31. Wani, S., Pull, S.R., Shaheen, N.J., Westhoff, B., Slehria, S., Bansal, A. et al. Esophageal adenocarcinoma in Barrett's esophagus after endoscopic ablative therapy: a meta-analysis and systematic review. Am J Gastroenterol 104, 502-513, doi:10.1038/ajg.2008.31 (2009).
32. Winawer, S. J., Zauber, A.G., Ho, M.N., O'Brien, M.J., Gottlieb, L.S., Sternberg, S.S. et al. Prevention of colorectal cancer by colonoscopic polypectomy. The National Polyp Study Workgroup. N Engl J Med 329, 1977-1981, doi:10.1056/NEJM199312303292701 (1993).
33. El-Serag, H. B. & Graham, D. Y. Routine polypectomy for colorectal polyps and ablation for Barrett's esophagus are intellectually the same. Gastroenterology 140, 386-388, doi:10.1053/j.gastro.2010.12.019 (2011).
34. Sampliner RE. Practice guidelines on the diagnosis, surveillance, and therapy of Barrett's esophagus: the Practice Parameters Committee of the American College of Gastroenterology. Am J Gastroenterol. 1998;93:1028–1032.
35. Peters, F. P., Brakenhoff, K.P., Curvers, W.L., Rosmolen, W.D., Fockens, P., Ten Kate, F.J. et al. Histologic evaluation of resection specimens obtained at 293 endoscopic resections in Barrett's esophagus. Gastrointest Endosc 67, 604-609, doi:10.1016/j.gie.2007.08.039 (2008).
36. Wani, S., Falk, G., Hall, M., Gaddam, S., Wang, A., Gupta, N. et al. Patients with nondysplastic Barrett's esophagus have low risks for developing dysplasia or esophageal adenocarcinoma. Clin Gastroenterol Hepatol 9, 220-227; quiz e226, doi:10.1016/j.cgh.2010.11.008 (2011).
37. Horvath, B., Singh, P., Xie, H., Thota, P.N., Allende, D.S., Pai, R.K. et al. Risk for esophageal neoplasia in Barrett's esophagus patients with mucosal changes indefinite for dysplasia. J Gastroenterol Hepatol 30, 262-267, doi:10.1111/jgh.12696 (2015).
38. Skacel, M., Petras, R.E., Gramlich, T.L., Sigel, J.E., Richter, J.E.., goldblum, J.R. The diagnosis of low-grade dysplasia in Barrett's esophagus and its implications for disease progression. Am J Gastroenterol 95, 3383-3387, doi:10.1111/j.1572-0241.2000.03348.x (2000).
39. Duits, L. C., Phoa, K.N., Curvers, W.L., Ten Kate, F.J., Meijer, G.A., Seldenrijk, C.A. et al. Barrett's oesophagus patients with low-grade dysplasia can be accurately risk-stratified after histological review by an expert pathology panel. Gut 64, 700-706, doi:10.1136/gutjnl-2014-307278 (2015).
40. Phoa, K. N., Van Vilsteren, F.G., Weusten, B.L., Bisschops, R., Schoon, E.J., Ragunath, K. et al. Radiofrequency ablation vs endoscopic surveillance for patients with Barrett esophagus and low-grade dysplasia: a randomized clinical trial. JAMA 311, 1209-1217, doi:10.1001/jama.2014.2511 (2014).
41. Hu, Y., Puri, V., Shami, V. M., Stukenborg, G. J. & Kozower, B. D. Comparative Effectiveness of Esophagectomy Versus Endoscopic Treatment for Esophageal High-grade Dysplasia. Ann Surg 263, 719-726, doi:10.1097/SLA.0000000000001387 (2016).
42. Dunbar, K. B. & Spechler, S. J. The risk of lymph-node metastases in patients with high-grade dysplasia or intramucosal carcinoma in Barrett's esophagus: a systematic review. Am J Gastroenterol 107, 850-862; quiz 863, doi:10.1038/ajg.2012.78 (2012).
43. Pennathur, A., Farkas, A., Krasinskas, A.M., Ferson, P.F., Gooding, W.E., Gibson, M.K. et al. Esophagectomy for T1 esophageal cancer: outcomes in 100 patients and implications for endoscopic therapy. Ann Thorac Surg 87, 1048-1054; discussion 1054-1045, doi:10.1016/j.athoracsur.2008.12.060 (2009).
44. Bergeron, E. J., Lin, J., Chang, A. C., Orringer, M. B. & Reddy, R. M. Endoscopic ultrasound is inadequate to determine which T1/T2 esophageal tumors are candidates for endoluminal therapies. J Thorac Cardiovasc Surg 147, 765-771: Discussion 771-763, doi:10.1016/j.jtcvs.2013.10.003 (2014).
45. Thosani, N., Singh, H., Kapadia, A., Ochi, N., Lee, J.H., Ajani, J. et al. Diagnostic accuracy of EUS in differentiating mucosal versus submucosal invasion of superficial esophageal cancers: a systematic review and meta-analysis. Gastrointest Endosc 75, 242-253, doi:10.1016/j.gie.2011.09.016 (2012).
46. Pouw, R. E., Heldoorn, N., Alvarez Herrero, L., Ten Kate, F.J., Visser, M., Busch, O.R. et al. Do we still need EUS in the workup of patients with early esophageal neoplasia? A retrospective analysis of 131 cases. Gastrointest Endosc 73, 662-668, doi:10.1016/j.gie.2010.10.046 (2011).
47. Manner, H., Pech, O., Heldmann, Y., May, A., Pohl, J., Behrens, A. et al. Efficacy, safety, and long-term results of endoscopic treatment for early stage adenocarcinoma of the esophagus with low-risk sm1 invasion. Clin Gastroenterol Hepatol 11, 630-635; quiz e645, doi:10.1016/j.cgh.2012.12.040 (2013).
48. Zehetner, J., DeMeester, S.R., Hagen, J.A., Ayazi, S., Augustin, F., Lipham, J.C. et al. Endoscopic resection and ablation versus esophagectomy for high-grade dysplasia and intramucosal adenocarcinoma. J Thorac Cardiovasc Surg 141, 39-47, doi:10.1016/j.jtcvs.2010.08.058 (2011)
49. Schmidt, H. M., Mohiuddin, K., Bodnar, A.M., El Lakis, M., Kaplan, S., Irani, S. et al. Multidisciplinary treatment of T1a adenocarcinoma in Barrett's esophagus: contemporary comparison of endoscopic and surgical treatment in physiologically fit patients. Surg Endosc, doi:10.1007/s00464-015-4621-z (2015).
50. Chang, E. Y., Morris, C.D., Seltman A.K., O'Rourke, R.W., Chan, B.K., Hunter, J.G. et al. The effect of antireflux surgery on esophageal carcinogenesis in patients with barrett esophagus: a systematic review. Ann Surg 246, 11-21, doi:10.1097/01.sla.0000261459.10565.e9 (2007).
51. Stefanidis, D., Hope, W.W., Kohn, G.P., Reardon, P.R., Richardson, W.S., Fanelli, R.D. Guidelines for surgical treatment of gastroesophageal reflux disease. Surg Endosc 24, 2647-2669, doi:10.1007/s00464-010-1267-8 (2010).
52. Singh, S., Garg, S. K., Singh, P. P., Iyer, P. G. & El-Serag, H. B. Acid-suppressive medications and risk of oesophageal adenocarcinoma in patients with Barrett's oesophagus: a systematic review and meta-analysis. Gut 63, 1229-1237, doi:10.1136/gutjnl-2013-305997 (2014).
53. Singh, S., Singh, A. G., Singh, P. P., Murad, M. H. & Iyer, P. G. Statins are associated with reduced risk of esophageal cancer, particularly in patients with Barrett's esophagus: a systematic review and meta-analysis. Clin Gastroenterol Hepatol 11, 620-629, doi:10.1016/j.cgh.2012.12.036 (2013).
54. Zhang, S., Zhang, X.Q., Ding, X.W., Yang, R.K., Huang, S.L., Kastelein, F. et al. Cyclooxygenase inhibitors use is associated with reduced risk of esophageal adenocarcinoma in patients with Barrett's esophagus: a meta-analysis. Br J Cancer 110, 2378-2388, doi:10.1038/bjc.2014.127 (2014).
55. Becq, A., Camus, M., Rahmi, G., de Parades, V., Marteau, P., Dray, X. et al. Emerging indications of endoscopic radiofrequency ablation. United European Gastroenterol J 3, 313-324, (2015).
56. Haidry, R. J., Dunn, J.M., Butt, M.A., Burnell,M.G., Gupta,

A., Green, S. et al. Radiofrequency ablation and endoscopic mucosal resection for dysplastic barrett's esophagus and early esophageal adenocarcinoma: outcomes of the UK National Halo RFA Registry. Gastroenterology 145, 87-95, doi:10.1053/j.gastro.2013.03.045 (2013).
57. Allen, B., Kapoor, N., Willert, R., McEwan, H., Fullarton, G., Penman, I. et al. Endoscopic ablation of Barrett's neoplasia with a new focal radiofrequency device: initial experience with the Halo60. Endoscopy 44, 707-710, doi:10.1055/s-0032-1309903 (2012).
58. Shaheen , N. J., Sharma, P., Overholt, B.F., Wolfsen, H.C., Sampliner, R.E., Wang, K.K. et al. Radiofrequency Ablation in Barrett's Esophagus with Dysplasia. New England Journal of Medicine 360, 2277-2288, doi:doi:10.1056/NEJMoa0808145 (2009)
59. Shaheen, N. J., Overholt, B.F., Sampliner, R.E., Wolfsen, H.C., Wang, K.K., Fleischer, D.E. et al. Durability of radiofrequency ablation in Barrett's esophagus with dysplasia. Gastroenterology 141, 460-468, doi:10.1053/j.gastro.2011.04.061 (2011).
60. Fleischer, D. E., Overholt, B.F., Sharma, V.K., Reymunde, A., Kimmey, M.B., Chuttani, R. et al. Endoscopic ablation of Barrett's esophagus: a multicenter study with 2.5-year follow-up. Gastrointest Endosc 68, 867-876, doi:10.1016/j.gie.2008.03.008 (2008).
61. Fleischer, D. E., Overholt, B.F., Sharma, V.K., Reymunde, A., Kimmey, M.B., Chuttani, R. et al. Endoscopic radiofrequency ablation for Barrett's esophagus: 5-year outcomes from a prospective multicenter trial. Endoscopy 42, 781-789, doi:10.1055/s-0030-1255779 (2010).
62. Shaheen, N. J., Peery, A.F., Hawes, R.H., Rothstein, R.I., Spechler, S.J., Galanko, J.A. et al. Quality of life following radiofrequency ablation of dysplastic Barrett's esophagus. Endoscopy 42, 790-799, doi:10.1055/s-0030-1255780 (2010).
63. Das, A., Wells, C., Kim, H.J., Fleischer, D.E., Crowell, M.D., Sharma, V.K. An economic analysis of endoscopic ablative therapy for management of nondysplastic Barrett's esophagus. Endoscopy 41, 400-408, doi:10.1055/s-0029-1214612 (2009).
64. Caillol, F., Bories, E., Pesenti, C., Poizat, F., Monges, G., Guiramand, J. et al. Radiofrequency ablation associated to mucosal resection in the oesophagus: experience in a single centre. Clin Res Hepatol Gastroenterol 36, 371-377, doi:10.1016/j.clinre.2012.01.004 (2012).
65. Okoro, N. I., Tomizawa, Y., Dunagan, K.T., Lutzke, L.S., Wang, K.K., Prasad, G.A. Safety of prior endoscopic mucosal resection in patients receiving radiofrequency ablation of Barrett's esophagus. Clin Gastroenterol Hepatol 10, 150-154, doi:10.1016/j.cgh.2011.10.030 (2012).
66. Haidry, R. J., Butt, M.A., Dunn, J.M., Gupta, A., Lipman, G., Smart, H.L. et al. Improvement over time in outcomes for patients undergoing endoscopic therapy for Barrett's oesophagus-related neoplasia: 6-year experience from the first 500 patients treated in the UK patient registry. Gut 64, 1192-1199, doi:10.1136/gutjnl-2014-308501 (2015).
67. van Vilsteren, F. G., Pouw, R.E., Seewald, S., Alvarez Herrero, L., Sondermeijer, C.M., Visser, M. et al. Stepwise radical endoscopic resection versus radiofrequency ablation for Barrett's oesophagus with high-grade dysplasia or early cancer: a multicentre randomised trial. Gut 60, 765-773, doi:10.1136/gut.2010.229310 (2011).
68. Akiyama, J., Marcus, S. N. & Triadafilopoulos, G. Effective intra-esophageal acid control is associated with improved radiofrequency ablation outcomes in Barrett's esophagus. Dig Dis Sci 57, 2625-2632, doi:10.1007/s10620-012-2313-2 (2012).
69. Krishnan, K., Pandolfino, J.E., Kahrilas, P.J., Keefer, L., Boris, L., Komanduri, S. Increased risk for persistent intestinal metaplasia in patients with Barrett's esophagus and uncontrolled reflux exposure before radiofrequency ablation. Gastroenterology 143, 576-581, doi:10.1053/j.gastro.2012.05.005 (2012).
70. Kahaleh, M., Van Laethem, J. L., Nagy, N., Cremer, M. & Deviere, J. Long-term follow-up and factors predictive of recurrence in Barrett's esophagus treated by argon plasma coagulation and acid suppression. Endoscopy 34, 950-955, doi:10.1055/s-2002-35847 (2002).
71. Ferraris, R., Fracchia, M., Foti, M., Sidoli, L., Taraglio, S., Vigano, L. et al. Barrett's oesophagus: long-term follow-up after complete ablation with argon plasma coagulation and the factors that determine its recurrence. Aliment Pharmacol Ther 25, 835-840, doi:10.1111/j.1365-2036.2007.03251.x (2007).
72. Orman, E. S., Kim, H.P., Bulsiewicz, W.J., Cotton, C.C., Dellon, E.S., Spacek, M.B. et al. Intestinal metaplasia recurs infrequently in patients successfully treated for Barrett's esophagus with radiofrequency ablation. Am J Gastroenterol 108, 187-195; quiz 196, doi:10.1038/ajg.2012.413 (2013).
73. Pasricha, S., Bulsiewicz, W.J., Hathorn, K.E., Komanduri, S., Muthusamy, V.R., Rothstein, R.L. et al. Durability and predictors of successful radiofrequency ablation for Barrett's esophagus. Clin Gastroenterol Hepatol 12, 1840-1847 e1841, doi:10.1016/j.cgh.2014.04.034 (2014).
74. Cotton, C. C., Wolf, W.A., Pasricha, S., Li, N., Madanick, R.D., Spacek, M.B. et al. Recurrent intestinal metaplasia after radiofrequency ablation for Barrett's esophagus: endoscopic findings and anatomic location. Gastrointest Endosc 81, 1362-1369, doi:10.1016/j.gie.2014.12.029 (2015).
75. Ganz, R. A., Overholt,B.F., Sharma, V.K., Fleischer, D.E, Shaheen, N.J., Lightdale, C.J. et al. Circumferential ablation of Barrett's esophagus that contains high-grade dysplasia: a U.S. Multicenter Registry. Gastrointest Endosc 68, 35-40, doi:10.1016/j.gie.2007.12.015 (2008).
76. Sharma, V. K., Jae Kim, H., Das, A., Wells, C.D., Nguyen,C.C., Fleischer, D.E. Circumferential and focal ablation of Barrett's esophagus containing dysplasia. Am J Gastroenterol 104, 310-317, doi:10.1038/ajg.2008.142 (2009).
77. Velanovich, V. Endoscopic endoluminal radiofrequency ablation of Barrett's esophagus: initial results and lessons learned. Surg Endosc 23, 2175-2180, doi:10.1007/s00464-009-0364-z (2009).
78. Lyday, W. D., Corbett,F.S., Kuperman, D.A., Kalvaria, I., Mavrelis, P.G., Shughoury, A.B. et al. Radiofrequency ablation of Barrett's esophagus: outcomes of 429 patients from a multicenter community practice registry. Endoscopy 42, 272-278, doi:10.1055/s-0029-1243883 (2010).
79. Pouw, R. E., Wirths, K., Eisendrath, P., Sondermeijer, C.M., Ten Kate, F.J., Fockens, P. et al. Efficacy of radiofrequency ablation combined with endoscopic resection for barrett's esophagus with early neoplasia. Clin Gastroenterol Hepatol 8, 23-29, doi:10.1016/j.cgh.2009.07.003 (2010).
80. Bergman, J. J., Zhang, Y.M., He, S., Weusten, B., Xue, L., Fleischer, D.E. et al. Outcomes from a prospective trial of endoscopic radiofrequency ablation of early squamous cell neoplasia of the esophagus. Gastrointest Endosc 74, 1181-1190, doi:10.1016/j.gie.2011.05.024 (2011).
81. Zemlyak, A. Y., Pacicco, T., Mahmud, E.M., Tsirline, V.B., Belyansky, I., Walters, A. et al. Radiofrequency ablation offers a reliable surgical modality for the treatment of Barrett's esophagus with a minimal learning curve. Am Surg 78, 774-778 (2012).
82. Bulsiewicz, W. J., Kim, H.P., Dellon, E.S., Cotton, C.C., Pasricha, S., Madanick, R.D. et al. Safety and efficacy of endoscopic mucosal therapy with radiofrequency ablation for patients with neoplastic Barrett's esophagus. Clin Gastroenterol Hepatol 11, 636-642, doi:10.1016/j.cgh.2012.10.028 (2013).
83. Phoa, K. N., Pouw, R.E., Van Vilsteren, F.G., Sondermeijer, C.M., Ten Kate, F.J., Visser, M. et al. Remission of Barrett's esophagus with early neoplasia 5 years after radiofrequency ablation with endoscopic resection: a Netherlands cohort study. Gastroenterology 145, 96-104, doi:10.1053/j.gastro.2013.03.046 (2013).
84. Pasricha, S., Bulsiewicz, W.J., Hathorn, K.E., Komanduri, S., Muthusamy, V.R., Rothstein, R.I. et al. Durability and predictors of successful radiofrequency ablation for Barrett's esophagus. Clin Gastroenterol Hepatol 12, 1840-1847 e1841, doi:10.1016/j.cgh.2014.04.034 (2014).
85. He, S., Bergman, J., Zhang, Y., Weunsten, B., Xue, L., Qin, X. et al. Endoscopic radiofrequency ablation for early esophageal squamous cell neoplasia: report of safety and effectiveness from a large prospective trial. Endoscopy 47, 398-408, doi:10.1055/s-0034-1391285 (2015).