Radiofrequency Ablation for Barrett’s Esophagus High-Volume Center Initial Results

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INTRODUCTION

Worldwide increasing incidence of esophageal adenocarcinoma (EAC) made Barrett’s esophagus (BE) today an evaluating and controversial topic. BE is defined as a columnar epithelium within the tubular esophagus, macroscopically visible on endoscopic examination, and proven by histological presence of goblet cells, representing the specialized intestinalized metaplastic epithelium. Recognized as a premalignant lesion, due to its potential to evolve through the metaplasia-dysplasia sequence into EAC, BE should be carefully monitored and treated. Surveillance is recommended in all patients with BE, and it should be adapted to histological grade. Prospective trials have shown benefit of surveillance protocols for BE, in the term of reaching the early diagnosis of high grade dysplasia (HGD) and EAC, but also with regard to improved survival with early stage EAC. Still, there are some studies that question surveillance programs, in the term of their effectiveness and cost-benefits. In patients with chronic gastroesophageal reflux disease (GERD) and resulting BE, treatment with proton pump inhibitors (PPI) may lead to symptom resolution, but the risk of BE progression remains, although it is likely to be reduced. Antireflux surgery (ARS) can successfully control the pathologic gastroesophageal reflux (GER), contrary to medications both acid and non-acid, and it has been shown that BE can even regress after ARS. Still, several less invasive endoscopic methods were introduced in order to completely eradicate the presence of this potentially premalignant lesion.

All endoscopic procedures performed in the treatment of BE could be divided into endoscopic mucosal resection and mucosal ablative techniques. In recent years endoscopic radiofrequency ablation (RFA) for BE was proven to be a safe and successful treatment modality. Procedure is characterized with extremely low complication rate, and high rate of complete BE eradication. A highly...
respected multicentric prospective sham-controlled trial proved RFA to be successful in the treatment of Barrett’s dysplasia in 90.5% of patients.12

The goal of this study is to present the initial early results of our Department in the treatment of BE with endoscopic RFA.

METHODS

The study was conducted at the Department of Esophageal Surgery, University Hospital for Digestive Surgery, Clinical Center of Serbia, from January 2010 until March 2012, and was approved by Hospital Board and Ethics Committee. In this study all included patients had macroscopically visible BE on endoscopy, proven by histological presence of goblet cells in biopsy specimens. Endoscopy, using narrow band imaging (NBI) and pathology reports were carefully reviewed before the patients entered the study. All patients included in this study were present with typical GERD symptoms and high incidence of erosive esophagitis at endoscopy. Endoscopically BE was classified according to C and M Prague criteria.

After the confirmation of BE, patients were submitted to standardized pre-procedural protocol. This protocol included: symptom questionnaire, stationary esophageal manometry, 24 hour esophageal pH-metry or impedance-pH testing. After diagnosis was made all patients were treated with 80 mg of esomeprazol daily for a period of one month.

The RFA procedure was conducted with HALO 90 and 360 systems (Barrx Medical Inc., Sunnyvale, CA) (Figure 1). HALO RFA system consists of generator unit which produces energy in dose of 10-12Js/cm², applied trough the catheters covering approximately one forth of esophageal circumference (HALO 90), or whole esophageal circumference (HALO 360). HALO 90 catheter is mounted onto the endoscope, while balloon based HALO 360 catheter is introduced over the endoscopically placed guidewire. Procedure was carried in analgosedation for HALO 90, and general endotracheal anesthesia for HALO 360 procedure. During the initial RFA, maximal extent of circumferentially treated BE mucosa was 5 cm. If the patient was presented with longer circumferential segments of BE, ablation was conducted in two consecutive procedures, 6 weeks apart. After the RFA procedure all patients were treated with 40 mg of esomeprazol twice daily (b.i.d) and procinetics three times a day (t.d.s) for a period of at least 6 weeks.

Follow-up protocol included: symptom questionnaire, upper GI endoscopy, and stationary esophageal manometry. For all post-RFA endoscopies we used endoscopic NBI in order to assess the presence of residual metaplastic or dysplastic epithelium. In case of residual BE another RFA procedure was carried out, until the complete eradication of BE was achieved. One year after the procedure if no visible macroscopic BE was present, biopsy specimens were taken from the level of esophagogastric junction (EGJ) and distal esophagus, in order to establish pathohistological existence of intestinal metaplasia (IM) or low grade dysplasia (LGD).

The primary goal of this study was to evaluate the success of BE eradication with RFA on the short term follow-up. Secondary goals were to compare the symptom scores and functional diagnostics data before and after the RFA procedure. We also evaluated the upper GI endos-
copy data after the RFA procedure, not only in the term of residual BE, but also in the term of post-procedural esophageal inflammatory changes.

Data are expressed in mean and median values. We used Fisher’s exact test, Student’s t-test and Kruskal-Wallis one-way analysis of variance test. Point of statistical significance was set on 0.05. For the purpose of statistical analyzes we used SPSS, version 20.0.0.

RESULTS

In this study we included a total of first 40 pts treated with RFA for BE at our Department. All patients met inclusion criteria and were submitted to follow-up protocols. Basic demographic data are shown in Table 1.

Mean duration of GERD symptoms in this group of patients was 5.2 ±2.2, while the mean duration of PPI therapy was 1.8 ±0.9 years. Cumulative symptom score mean values were 6.1, and the heartburn was a leading symptom in the majority of patients (mean values 2.1). Pre-procedural endoscopy revealed high incidence of erosive esophagitis (92.5 %): according to LA classification 23 patients were presented with grade A, while 9 and 5 patients were presented with grade B and C esophagitis respectively. Mean value of BE circumferential length (C) was 1.61 cm (maximal 10 cm), while the mean value of proximal BE extent (M) was 3.29 cm (maximal 11 cm). On definitive biopsy specimens IM was present in 32, while 8 patients had LGD proven with two consecutive biopsies. HALO 90 was the initial treatment modality in 28, while HALO 360 was initially done in 12 patients. Repeated RFA treatment was conducted in 7 patients so far, mainly due to the length of BE itself (no more than 5 cm of RFA was performed in one session) or because of the presence of the remaining small inlets of BE mucosa. In 5 of them HALO 90 was the method of choice, while in 2 patients repeated HALO 360 procedure was performed. In 3 patients additional third RFA procedure had to be done. The overall number of RFA procedures was 50, while the mean number of RFA procedures per patient was 1.25. (Table 2)

We did not encounter esophageal perforation or hemorrhage during the RFA procedure for BE. Retrosternal pain was present in 23 patients in post-procedural period (mean duration 13±4.1 days), while mild dysphagia occurred in 11 patients (mean duration 11±3.2 days).

Three months after the RFA mean values of cumulative symptom score dropped significantly (mean value 3.1, p<0.05), while the mean values of heartburn score also decreased to 0.8 (p<0.05). The manometric tracings three months after the RFA procedure revealed statistically non-significant decrease in a mean lower esophageal sphincter (LES) resting pressure values as well as in the mean distal esophageal contraction amplitudes. (Table 3)

One year follow-up after complete macroscopically visible BE eradication was accomplished in 26 patients. In these patients regular biopsy specimens of EGJ revealed presence of IM in 3 of them (11.53%), and these patients will be submitted only to repeated HALO 90 procedure, while no patients were present with LGD.

So far, in 19 patients after the RFA procedure a laparoscopic Nissen fundoplication (NF) was performed 3 to 6 months after complete BE eradication. Board approved study protocol predicts further comparison of patients with BE on continuous PPI treatment and those with additional NF after RFA.

DISCUSSION

BE is defined as specialized intestinal metaplasia, containing goblet cells, and it is a recognized precursor of esophageal adenocarcinoma. Rapid raise of EAC incidence, has led to the development of different surveillance and treatment strategies of BE, while the HALO RFA represents the most recent one of endoscopic treatment modalities. So far, HALO RFA of BE has been proven as ve-

<table>
<thead>
<tr>
<th>TABLE 2</th>
<th>HALO RADIOFREQUENCY ABLATION OF BARRETT’S ESOPHAGUS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barett’s Esophagus</td>
<td>Patients</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Intestinal metaplasia</td>
<td>32</td>
</tr>
<tr>
<td>Low grade dysplasia</td>
<td>8</td>
</tr>
<tr>
<td>Overall</td>
<td>40</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>TABLE 3</th>
<th>PRE AND THREE MONTHS POST-RFA MANOMETRIC TRACINGS IN PATIENTS WITH BE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before RFA</td>
<td>After RFA</td>
</tr>
<tr>
<td>LES resting pressure</td>
<td>6.2±/-3.1 mmhg</td>
</tr>
<tr>
<td>Distal esophageal amplitudes</td>
<td>48.3±/-19.3 mmHg</td>
</tr>
</tbody>
</table>
ry safe and effective in complete healing of esophageal metaplastic or dysplastic epithelium.\textsuperscript{13,14} HALO RFA procedure is linked with extremely low incidence of esophageal perforation or hemorrhage during the course of procedure. Energy that is delivered through the process of ablation is strictly limited to 10-12 Js/cm\textsuperscript{2}, therefore preventing deeper damage from the level of muscularis mucosa. Opposed to esophageal mucosal resection, occurrence of post-procedural esophageal strictures is very rare.\textsuperscript{15}

In a short period of time due to excellent results obtained in various settings, HALO RFA procedure has established itself as a method of choice for the treatment of BE in majority of specialized centers. Our early experiences with HALO RFA procedure are more than satisfying and were linked with no serious complications. Side effects of procedure such as retrosternal pain or mild dysphagia had early resolution, and represented no serious burden to patients after HALO RFA procedure.

We would like to emphasize that all patients treated with RFA and included in this study protocol had long history of GERD, were infrequently treated with PPI for a long period of time, and were often endoscopically presented with reflux esophagitis. In our study protocol we approached the HALO RFA procedure only after the complete resolution of reflux esophagitis was achieved, while the symptom control with PPI was excellent in majority of patients. In this study, functional diagnostics showed initially low values of distal esophageal contraction amplitudes as well as LES resting pressures in most of the BE patients, but without statistically significant decrease in a post-RFA period. We can assume that these slight decreases were due to a temporary neuromuscular reaction to radiofrequency energy, indicating that this procedure does not alter the functional setting of the body of the esophagus and LES. Special emphasis during the procedure was given upon the ablation of esophago-gastric junction (EGJ), which could explain the low rate of recurrent/residual IM after one year (11.53%). In the study of Vaccaro et al. cumulative incidence of newly detected IM one year after complete eradication of BE was 25.9%.\textsuperscript{16} All cases of recurrent IM were detected at the level of EGJ, and were not macroscopically visible.

Today, there are still several unresolved issues regarding the HALO RFA procedure. One of them is should RFA be routinely used in the treatment of BE with only metaplastic or dysplastic epithelium.\textsuperscript{13,14} In conclusion, HALO RFA procedure is safe and effective in complete healing of esophageal metaplastic or dysplastic epithelium.\textsuperscript{13,14}

Other issue concerns the further treatment protocol for patients treated with RFA. RFA procedure successfully eradicate the BE but the cause, chronic gastroesophageal reflux still remains. It has been documented that patients with BE are presented with increased pathologic GER even on high dose PPI treatment, predominantly due to a combined (acid and bile) type of reflux itself.\textsuperscript{22} There are several reports about an additional antireflux surgery after RFA, as a definitive treatment for the resolution of chronic reflux problems.\textsuperscript{23,24} There is even a study showing that HALO RFA and Nissen procedure can safely be done as combined procedures.\textsuperscript{25} At our Department we already performed a laparoscopic Nissen fundoplication in 19 patients after HALO RFA and complete BE eradication. We estimate that the optimal time for surgery is more than three months after the RFA procedure. Patients in whom NF was performed and those on continuous PPI therapy only, will be included in our future study protocol. In this study we shall compare the symptomatic and objective structural and functional diagnostic data of these two groups of patients.

In conclusion, HALO RFA procedure is safe and effective in the treatment of patients with BE. Procedure does not lead to esophageal function impairment, and gives no long term and serious side effects. On the short term, rate of complete BE resolution is high, and no progression of IM or LGD has been shown in this group of patients. Further treatment options for BE patients treated successfully with RFA are to be enlightened in future, throughout the surveillance protocols, indicating laparoscopic NF as a treatment modality of choice.

**SUMMARY**

**RADIOFREKVENTNA ABLACIJA BARRETT-OVOG JEDNJAKA**

Uvod: Barrett-ov jednak (BJ) predstavlja dokazani proražnik adenokarcinoma jednjaka. Do sada su predloženi mnogobrojni veoma različiti protokoli lečenja i praćenja bolesnika sa BJ. Uvodjenje radiofrekventne ablacije (RFA) u lečenju BJ dovelo je do sasvim drugačijeg pristupa ovom problemu sa inicijalno odličnim rezultatima.


Rezultati: Prosečna cirkumferentna dužina BJ je iznosila 1.61, dok je maksimalna bila 3.29 cm. Tokom procedure nije bilo perforacije jednjaka niti krvenja. Nakon intervencije 23 bolesnika su osećali retrosternalni bol, dok je
Radiofrequency ablation for Barrett’s esophagus: high-volume center initial results

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11 imalo disfagične smetnje. Tri meseca nakon RFA prosečne vrednosti kumulativnog zbiра simptoma i gorušice su značajno smanjene (p<0.05). Funkcionalna diag nostika nije ukazala na statistički značajan pad u vred nostima donjeg ezofagealnog sfiktera ili amplituda kontrakcija distalnog jednjaka. U periodu od godinu dana pruženo je ukupno 26 bolesnika kod kojih je postojala kompletna makroskopska eradikacija BJ. Nakon kompletne eradikacije BJ, do sada je kod 19 bolesnika načinjena laparoskopska Nissen-ova operacija.

Zaključak: HALO RFA predstavlja sigurnu i veoma efikasnu metodu u lečenju BJ. HALO RFA ne dovodi do oštećenja funkcije jednjaka ili dugotrajnijih neželjenih efekata.

Ključne reči: Barrett-ov jednjak, Radiofrekventna ablacija, Antirefluksnia hiruršija

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