Single step treatment using radiofrequency ablation and endoscopic resection for Barrett esophagus containing early neoplasia .

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To test the use of RFA and ER in a single endoscopic session in 20 consecutive patients with a BE containing visible abnormalities with HGD or EC upon biopsy.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Malignant and unspecified neoplasms gastrointestinal NEC
Study type	Interventional

Summary

ID

NL-OMON33359

Source
ToetsingOnline

Brief title
Radiofrequency ablation and endoscopic resection: one treatment

Condition

- Malignant and unspecified neoplasms gastrointestinal NEC

Synonym
Barrett's esophagus, early cancer

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,BARRx Medical Inc,

540 Oakmead Parkway, Sunnyvale CA 94085,Industrie

Intervention

Keyword: Barrett's esophagus, Dysplasia, Endoscopic resection, Radiofrequency ablation

Outcome measures

Primary outcome

1. The rate of complete remission of HGD and EC in all biopsies obtained at 12 months follow-up.

2. The rate of complete remission of BE, defined as the endoscopic absence of columnar lined epithelium upon inspection with NBI and the absence of intestinal metaplasia in all biopsy specimens obtained at 12 months follow-up.

Secondary outcome

3. The rate of acute (i.e. < 3 days) complications after therapeutic procedures.

4. The rate of late (such as esophageal stenosis) complications occurring during the treatment phase or during follow-up.

5. The number of endoscopic therapeutic procedures.

6. The frequency, severity, and duration of patient*s symptoms after the first therapeutic session as assessed with standardised questionnaires and patient diaries.

Study description

Background summary

Endoscopic resection (ER) and radiofrequency ablation (RFA) are effective treatment modalities for high-grade dysplasia (HGD) and early cancer (EC) in Barrett*s esophagus (BE).
ER of early BE neoplasia allows for resection deep into the submucosa, which

not only effectively removes superficial lesions but also permits accurate histological staging. The histological evaluation of ER specimens is imperative for proper patient selection: patients with mucosal lesions can be treated endoscopically, whereas those with submucosal cancers are referred for surgery given their significant risk of local lymph node metastasis.
RFA effectively removes BE mucosa but has only been used for flat type mucosa without visible abnormalities since these require ER for effective removal and staging.
Compared to ER, RFA is a relatively easy endoscopic procedure with a low risk of complications and no significant esophageal scarring.
The combined treatment of ER and RFA currently requires two separate treatment sessions. Generally, an interval of 6-8 weeks is used to allow the esophagus to heal before RFA is applied.
Esophageal scarring after ER may, however, hamper the efficacy and safety of subsequent RFA sessions. After ER, it may be more difficult to bring the ablation balloon in full contact with the remaining BE. In addition, widespread ER may cause so much stricturing that inflation of the balloon catheter may cause esophageal laceration. For this reason most studies on the combined treatment with ER and RFA have restricted the maximum extent of ER prior to RFA to < 50% of the circumference and <2 cm in longitudinal length.

Study objective

To test the use of RFA and ER in a single endoscopic session in 20 consecutive patients with a BE containing visible abnormalities with HGD or EC upon biopsy.

Study design

Inclusion criteria:
1. Age between 18 and 85 years inclusive.
2. BE with a minimal circumferential extent of 2 cm.
3. An endoscopically visible abnormality of type 0-I, 0-IIa, 0-IIc or a combination thereof, irrespective of its size.
4. A biopsy proven histological diagnosis of HGD and/or EC on two separate endoscopic sampling procedures.
5. HGD, G1 or G2 cancer in the endoscopic resection specimens, without involvement of the deeper resection margins, no lymphatic invasion, and a maximum infiltration depth into the submucosa <500µm.
6. Written informed consent.

Exclusion criteria:
1. A BE with a maximum extent >12 cm.
2. Any prior endoscopic treatment for esophageal adenocarcinoma of BE associated neoplasia.
3. Signs of local or distant metastasis on EUS (EUS is obligatory).
4. Signs of distant metastasis on CT-scan of thorax and/or abdomen (optional

for mucosal lesions).
5. Any of the following findings in any of the ER specimens: G3 or G4 tumor differentiation; lymphatic invasion; infiltration into the submucosa >500µm, a positive deeper resection margin.
6. Endoscopic signs of esophageal varices.
7. Esophageal stenosis not allowing passage of a therapeutic endoscope with an ER-cap.
8. Prior esophageal surgery (except fundoplication).
9. Use of any anticoagulant therapy that can not be discontinued between one week before and 1 week after every treatment session.

Procedures:
Endoscopic work-up:
Prior to the first therapeutic endoscopy all patients will undergo 2 endoscopies with targeted (i.e. 2 biopsies per lesion) and random biopsies (i.e. 4QBx/1-2 cm).
Endoscopic ultrasound (EUS) will be performed using a radial scanning electronic EUS endoscope, supplemented with EUS-FNA in case suspicious lymph nodes are detected.
CT scan of thorax/abdomen is only required for those patients who show submucosal invasion.

Endoscopic treatment protocol (see flow chart):
All patients will undergo a circumferential ablation using the HALO360+ system according to current guidelines, followed by endoscopic resection of any visible abnormality in the BE during the same procedure. Prior to the ablation, the area to be resected will be marked by placing electrocoagulation markers. After the ablation, the delineated area will be resected using either the multi-band mucosectomy technique of the ER-cap technique, until all visible markers have been removed.
The second ablation session is scheduled after 3 months followed by 2-monthly ablation sessions until all endoscopically visible BE has been removed. A maximum number of 2 HALO360+ (for circumferential ablation) and 3 HALO90 sessions (for focal ablation of residual islands) are allowed.
In case Barrett mucosa persists after completing the maximum number of ablation sessions, an ER will be performed as an *escape*procedure to achieve complete removal. An ER is also allowed if during the treatment phase visible abnormalities are identified in the original BE.
In case complete endoscopic regression of the BE is observed, 4-quadrant random biopsies will be obtained at 1-2 cm intervals throughout the original BE. In addition, 4-quadrant random biopsies will be obtained immediately distal (i.e. < 5-mm) of the neo-squamocolumnar junction.
After complete endoscopic and histological eradication of HGD, EC and BE has been documented, patients will undergo follow-up at 6 and 12 months, and annually thereafter, using the aforementioned biopsy protocol.
Focal ablation sessions with the HALO90 system and all follow-up endoscopies will be performed with high-resolution endoscopy and narrow-band imaging.

Apart from the first treatment session, in which RFA and ER are combined, the treatment protocol and follow-up regimen are identical to those of 5 previous cohort studies by our group.

Post-treatment care and medication
After all therapeutic procedures, patients will be observed in the recovery room for 2-4 hours and subsequently discharged with further instructions concerning diet, acid suppressant therapy, and the use of analgetics. After the first therapeutic session, the frequency, severity, and duration of symptoms will be assessed by standardised questionnaires and patient diaries.
Patients will be contacted by telephone within 72 hours and will be rescheduled for repeat procedures or follow-up endoscopies according to the aforementioned schedule.

Histology
All pre-treatment histology, all ER specimens, and all follow-up biopsies will be routinely processed and evaluated by a senior gastroenterologist. For the purpose of this study, all materials will be reviewed by an expert GI-pathologist with extensive experience in this field.

Intervention

Resection of visible lesion with high grade dysplasia and/or early cancer and total eradication of Barrett's esophagus.

Study burden and risks

We anticipate that ER immediately after RFA will not be associated with a higher risk for complications. In fact, the risk for perforation, the most feared complication of ER, is likely to be reduced due to the slight mucosal thickening that occurs immediately after RFA.
RFA of visible lesions prior to their resection may effect the histological evaluation of the superficial part of the resected specimen. The main purpose of the histological evaluation of ER specimens, however, is the evaluation of the deeper mucosal and superficial submucosal layers, which are left undamaged by the RFA.
This allows for a combined treatment which otherwise would require 2 separate procedures but more importantly, it preserves the diagnostic and therapeutic efficacy of ER but prevents that RFA is hampered by esophageal scarring after the ER. If this treatment regimen is found to be effective it will also allow patients with larger visible abnormalities to be treated with the combination of ER and RFA.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Age 18-85 years;
- Minimum circumferential extent of Barrett's of 2cm prior to treatment
- Endoscopic visible abnormality of type 0-I,0-IIa, 0-IIc or a combination therof.
- Biopsy proven High grade dysplasia (HGD) or Early cancer (EC) on two seperate endoscopic sampling procedures.
- Written informed consent

Exclusion criteria

1. Barrett's extent of >12cm
2. Any prior endoscopic treatment for esophageal adenocarcinoma of BE associated

neoplasia.
3. Signs of local or distant metastasis on EUS (EUS is obligatory).
4. Signs of distant metastasis on CT-scan of thorax and/or abdomen (optional for mucosal lesions).
5. Any of the following findings in any of the ER specimens: G3 or G4 tumor differentiation; lymphatic invasion; infiltration into the submucosa >500µm, a positive deeper resection margin.
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Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	18-09-2009
Enrollment:	20
Type:	Actual

Medical products/devices used

Generic name:	HALO Radiofrequency Ablation System
Registration:	Yes - CE intended use

Ethics review

Approved WMO

Application type:	First submission

Review commission: METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL27066.018.09