Advances in imaging and endoscopic therapy in Barrett’s esophagus
Alvarez Herrero, L.

Citation for published version (APA):
Alvarez Herrero, L. (2014). Advances in imaging and endoscopic therapy in Barrett’s esophagus

General rights
It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

Disclaimer/Complaints regulations
If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: http://uba.uva.nl/en/contact, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.

UvA-DARE (Digital Academic Repository)
Safety and efficacy of Multi-Band Mucosectomy in 1060 resections in Barrett’s Esophagus


Endoscopy. 2011 Mar;43(3):177-83
Part II: Endoscopic therapy in Barrett’s esophagus

Abstract

Introduction: Multi-Band Mucosectomy (MBM) is a relatively new technique for endoscopic resection (ER) in Barrett’s esophagus (BE). This ligate-cut technique uses a modified variceal band ligator allowing for 6 consecutive resections without prior submucosal lifting. Aim: To evaluate the safety of MBM and its efficacy for complete endoscopic removal of delineated target areas in BE. Methods: Prospective registration of all MBM procedures in BE was performed between Nov’04-Oct’09 in two hospitals. Prior to MBM, the target area was delineated with coagulation markings followed by ER until the delineated area was completely resected. Primary endpoints were acute (during procedure) plus early complications (<30 days) and the rate of complete endoscopic resection of the delineated target area. Results: 243 MBM procedures, with 1060 resections, were performed in 170 patients. MBM was performed for focal lesions (n=113), for BE removal as part of a (stepwise) radical ER protocol (n=117) and as escape treatment after radiofrequency ablation (n=13). Acute complications were 3% bleeding (endoscopically managed); no perforations occurred despite absence of submucosal lifting. Early complications consisted of 2% delayed bleeding (endoscopically managed); stenosis occurred in 48% of patients treated in a (stepwise) radical resection protocol, patients treated for focal lesions or escape treatment showed no stenosis. Complete endoscopic resection was achieved in 91% of the focal lesions, 86% when part of the (stepwise) radical ER protocol and 100% for escape treatment after radiofrequency ablation. Conclusions: MBM is a safe and effective technique for the removal of delineated target areas in BE.
Introduction

Endoscopic therapy is increasingly used for the treatment of early neoplasia in Barrett’s esophagus (BE). Endoscopic resection (ER) techniques are the basis of endoscopic therapy since histological evaluation of the resection specimen helps to select appropriate patients for further endoscopic treatment. Additional endoscopic treatment may consist of ablation or ER of the remaining BE. The most widely used ER technique in the esophagus is the ER-cap technique.[1-3] This technique requires submucosal lifting by injection of fluid and placement of a snare in the rim of a distally attached cap is necessary before each ER. This makes the ER-cap technique technically complicated and time consuming especially when multiple resections are required (i.e. piecemeal resection).

A new ER technique that overcomes these drawbacks is multi-band mucosectomy (MBM). [4-6] MBM uses a modified variceal band ligator that includes a transparent cap with six rubber bands and a modified control handle. The modification in the control handle allows the passage of a 7Fr snare through the accessory channel along the wires that are required for releasing the rubber bands. By suctioning mucosa into the cap and releasing a rubber band, a pseudopolyp is created. Subsequently the pseudopolyp can be resected with a snare without the need for prior lifting and without having to maneuver the snare in the rim of the cap. With one MBM kit, up to six resections can therefore be performed by repetitive suck-band-snare sequences. Despite its increasing popularity, limited data is available on the safety and efficacy of MBM in BE. During the past 5 years we have prospectively registered all ER procedures performed with MBM. The aim of this study was to evaluate the safety of MBM and to evaluate its efficacy for complete endoscopic removal of delineated lesions and areas in BE.

Methods

Patient selection

Patients were included if they underwent an MBM procedure in BE between November 2004 and October 2009 at the Academic Medical Center, Amsterdam or the Sint Antonius Hospital, Nieuwegein, the Netherlands. These two hospitals have an ongoing collaboration in the field of endoscopic detection and treatment of early neoplasia in the upper GI tract (see www.endosurgery.eu). All procedures relating to this collaboration were prospectively registered.
Endoscopic management

Patients underwent imaging endoscopies using standard or high resolution video endoscopy (GIF 140/160/180, Olympus Europe, Hamburg, Germany) and advanced imaging techniques such as narrow band imaging and autofluorescence endoscopy (GIF Q240/260Z, Olympus, Tokyo, Japan) and chromoendoscopy. Visible abnormalities were documented by recording their distance from the incisors and circumferential position followed by targeted biopsies and four-quadrant random biopsies every two cm of the BE. In case of high-grade intraepithelial neoplasia (HGIN) or cancer, patients underwent endoscopic ultrasonography (EUS) for lymph node inspection. If suspicious lymph nodes were present EUS-guided fine needle aspiration was performed.

Patients underwent MBM in BE for different indications: focal ER of a visible lesion; removal of BE as part of a (stepwise) radical resection protocol; and escape treatment of remaining BE after radiofrequency ablation (RFA).[7-10]

After focal lesion resection, further treatment was tailored for each patient depending on the histology of the ER specimens plus biopsies of the residual BE and co-morbidity. Additional endoscopic therapy of the remaining BE consisted of (stepwise) radical endoscopic resection, argon plasma coagulation (APC) and/or RFA, according to the protocols at that time.[10-13] Patients were referred for surgery in case endoscopic therapy was not considered appropriate. [14,15]

Multi-band mucosectomy kit

MBM was performed with the Duette™ Multi-Band Mucosectomy kit (Cook Medical, Limerick, Ireland). The Duette kit includes a modified variceal band ligator and a hexagonal snare. The modification of the variceal band ligator consists of a widened shaft of the control handle, allowing passage of 7Fr accessories into the working channel of the endoscope. A regular transparent cap with six rubber bands is attached to two wires. The wires can be fixed on the control handle by placing the cap onto the distal end of the endoscope and pulling the wires through the working channel with the help of a loading catheter delivered with the kit. In this way, rubber bands on the tip of the endoscope can be released by tensing the wires with the handle. A pseudopolyp is created when a rubber band is released while mucosa is sucked into the cap. Pseudopolyps can be resected with the hexagonal snare (7Fr or 5 Fr) that is included in the Duette kit.

Multi-band mucosectomy procedure

MBM procedures were performed under conscious sedation with intravenous administration of midazolam in combination with fentanyl or pethidine, generally as outpatient procedures.
After introducing the endoscope without the ligator and rinsing the esophagus with water, the lesion or area for ER was identified and the location was recorded (Figure 1). Delineation of the lesion or area was performed by placing coagulation markings in order to ensure radical resection since the endoscopic view during ER may be impaired because of the cap and possible bleeding. Markings were placed 2-5 mm outside the margins of the lesion using the tip of the hexagonal snare. Next, the endoscope was removed and the ligator was assembled on the endoscope. The wires were positioned in line with the working channel to keep them out of the endoscopic view. After introducing the endoscope with the ligator and identifying the delineated lesion or area, the mucosa was sucked into the cap and a rubber band was released when the cap was completely filled with mucosa (complete “red-out”). Since the rubber band is not strong enough to hold the muscularis propria, no lifting was used prior to resection. Pseudopolyps were removed immediately after rubber band ligation with the hexagonal snare using 45 Watt pure coagulation current (Erbotom ICC 200 and VIO 200D, ERBE Elektromedizin GmbH, Tuebingen, Germany). Resections were preferably performed below the rubber band. Resections were performed from distal to proximal or were started at the most suspicious part of the delineated area. A small overlap of 25% between adjacent resections was allowed, to prevent residual tissue bridges. Specimens resected during a piecemeal procedure were stored in the stomach until the piecemeal procedure was completed, i.e. when all resections were performed and all complications plus any bleeding were treated.

Bleeding obscuring the endoscopic view that did not resolve spontaneously was treated by focal coagulation of the bleeding vessel with the tip of the snare. If this did not stop the bleeding, additional therapy was performed with an electrosurgical hemostatic forceps (Coagrasper™, Olympus, Tokyo, Japan), a clip (Resolution™ Clip, Boston Scientific, Natick, Massachusetts) or adrenaline injection (1:10,000).

Resected specimens were retrieved from the stomach with a retrieval net (Roth Net®, US Endoscopy, Mentor, Ohio). Retrieved specimens were pinned down on paraffin with the mucosal side up, and fixed in formalin for histological evaluation. No attempts were made to reconstruct the specimen in case of piecemeal resection.

After the procedure patients were discharged after 2-4 hours of observation. Patients received ranitidine 300mg at bedtime and 5ml sulcrate suspension (200mg/ml) qid during 14 days in addition to the maintenance medication of esomeprazole 40 mg bid.
Part II: Endoscopic therapy in Barrett’s esophagus

Figure 1 Multi-Band Mucosectomy of a focal lesion (mucosal cancer) in a C<1M2 Barrett’s esophagus. Overview images showing the Barrett’s segment (A), the lesion (B) and the lesion in retroflexed position (C). After marking of the lesion (D) mucosa is sucked into the cap and a rubber band is released creating a pseudopolyp (E&F). The pseudopolyp is resected below the rubber band (G). Subsequently a second pseudopolyp is created (H) and resected, allowing a small overlap with the adjacent resection wound. After two resections, complete endoscopic resection is achieved as resections wounds are contiguous and no markings are left (I&J). Three months later the mucosa is completely healed with squamous epithelium showing only a scar at the 3 o’clock position (K=white light view; L=Narrow-Band Imaging).

Histology
ER specimens were cut into 2-mm slices, and cut in 4 μm slides for standard haemotoxilin & eosin staining.[16] During routine evaluation two pathologists classified abnormalities according to the WHO classification and disagreement was resolved by consensus after repeat combined evaluation.[17] In case of cancer, the following characteristics were assessed: tumor infiltration depth, tumor differentiation grade, presence of lymphatic or vascular infiltration, the radicality of the resection at the deep resection margins and, in case of en-bloc resections, the radicality of the lateral margins.

Follow-up
Patients were contacted by telephone within 24-48 hours and 2 weeks after the procedure to check for complications. After 2-3 months patients underwent a follow-up endoscopy with biopsies or additional endoscopic therapy.
Outcome parameters

The following parameters were assessed:

1) Number and severity of acute complications with MBM, i.e. complications occurring during the MBM procedure.
2) Number and severity of early complications after MBM, i.e. complications occurring within 30 days after the procedure.
3) Rate of complete endoscopic removal with MBM of the target area, defined as the complete removal of the delineated area including all markings as judged by the endoscopist during the MBM procedure. Additional therapy with APC for remaining margins or bridges was permitted to achieve complete endoscopic resection.

Severity of the complications was scored as follows: ‘mild’ (unplanned hospital admission, hospitalization ≤3 days, hemoglobin drop <3g/dL, no need for transfusion), ‘moderate’ (4-10 days hospitalization, ≤4 units blood transfusion, need for repeat endoscopic intervention, radiologic intervention), ‘severe’ (hospitalization >10 days, ICU admission, need for surgery, > 4 units blood transfusion, in the case of stenosis: >5 endoscopic dilatations, stent placement or incisional therapy) or ‘fatal’ (death attributable to procedure <30 days or longer in case of continuous hospitalization).[8]

Statistical analysis

Statistical analysis was performed with the Statistical Software Package version 16.0.2 for windows (SPSS, Chicago, Illinois, USA). For descriptive statistics, mean with standard deviation was used for variables with a normal distribution and the median with interquartile range (IQR) was used for variables with a skewed distribution. Confidence intervals of the proportions were calculated with the Confidence Interval Analysis package.[18] Categorical data were compared with the Chi square test or the Fisher exact test when expected cell values were too small. Continuous data that was not normally distributed were compared with the Mann-Whitney U test. Binary logistic regression was used to calculate the odds ratio for the association between clinically significant bleeding and the number of resection specimens per procedure.

Results

Patient and procedure characteristics

A total of 170 patients underwent 243 MBM procedures resulting in 1060 resections in the BE. Patients had a mean age of 67(±10) years, 150 were male and 20 female. Before any endoscopic
therapy, patients had a median BE length of C4M6 (IQR C1-7, M3-8). Hiatal hernia was present in 137 (81%) patients with a median length of 3cm (IQR 3-4).

MBM was performed for removal of focal lesions in the BE in 113 procedures; for removal of the whole BE as part of a (stepwise) radical ER protocol in 117 procedures; and for escape treatment after radiofrequency ablation in 13 procedures. The number of patients, procedures and resections per indication are shown in Table 1.

Table 1. Number of procedures and resections

<table>
<thead>
<tr>
<th>Indication</th>
<th>Patients</th>
<th>Procedures</th>
<th>Resections</th>
<th>Resections/procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Focal lesion</td>
<td>104(^a)</td>
<td>113 (47%)</td>
<td>311 (29%)</td>
<td>2 (IQR 1-4)</td>
</tr>
<tr>
<td>En-bloc</td>
<td>31</td>
<td>32</td>
<td>32</td>
<td>1 (IQR 1-1)</td>
</tr>
<tr>
<td>Piecemeal</td>
<td>76</td>
<td>81</td>
<td>279</td>
<td>3 (IQR 2-5)</td>
</tr>
<tr>
<td>(Stepwise) radical ER</td>
<td>69</td>
<td>117 (48%)</td>
<td>713 (67%)</td>
<td>5 (IQR 3-9)</td>
</tr>
<tr>
<td>Escape treatment</td>
<td>12</td>
<td>13 (5%)</td>
<td>36 (3%)</td>
<td>2 (IQR 1-3)</td>
</tr>
<tr>
<td>Total</td>
<td>170(^a)</td>
<td>243</td>
<td>1060</td>
<td>3 (IQR 2-6)</td>
</tr>
</tbody>
</table>

ER endoscopic resection
A: 3 patients underwent 1 en-bloc and 1 piecemeal procedure at different time points
B: 15 patients underwent procedures for a combination of indications at different time points: 10 patients underwent a resection for a focal lesion and later on an additional stepwise radical ER, and 5 patients underwent a resection for a focal lesion and at a later stage (after radiofrequency ablation) an escape treatment.

Pathology results showed cancer in the resection specimens in 97 (40%) procedures, HGIN in 47 (19%), LGIN in 35 (14%) and no intraepithelial neoplasia in 51 (21%) (Table 2).

Cancer infiltrated in the mucosa in 80/97 cases (73 with good/moderate differentiation and no lymphatic or vascular infiltration; 7 with poor differentiation and no lymphatic or vascular infiltration). Submucosal invading cancer was found in 16/97 cases (9 with good/moderate differentiation and no lymphatic or vascular infiltration; 7 with poor differentiation of which 3 with lymphatic or vascular infiltration). In 6 of these 16 cases the deep resection margin was tumor positive. In 1/97 infiltration depth could not be assessed by the pathologist because of tangential sectioning.

No pathology evaluation was available in 13/243 procedures (5%) because specimens were not retrieved (no clinical relevance in 10 as the largest lesion was already resected previously, no/small specimen in 3).
Table 2. Pathology results of MBM procedure subdivided for indication

<table>
<thead>
<tr>
<th></th>
<th>Focal lesion (n=113)</th>
<th>(Stepwise) radical ER (n=117)</th>
<th>Escape treatment (n=13)</th>
<th>Total (243)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer</td>
<td>71 (62.8%)</td>
<td>25 (21.4%)</td>
<td>1 (7.7%)</td>
<td>97 (39.9%)</td>
</tr>
<tr>
<td>HGIN</td>
<td>25 (22.1%)</td>
<td>21 (17.9%)</td>
<td>1 (7.7%)</td>
<td>47 (19.3%)</td>
</tr>
<tr>
<td>LGIN</td>
<td>9 (7.9%)</td>
<td>24 (20.5%)</td>
<td>2 (15.4%)</td>
<td>35 (14.4%)</td>
</tr>
<tr>
<td>No IN</td>
<td>7 (6.2%)</td>
<td>35 (29.9%)</td>
<td>9 (69.2%)</td>
<td>51 (21.0%)</td>
</tr>
<tr>
<td>No pathology</td>
<td>1 (0.9%)</td>
<td>12 (10.3%)</td>
<td>-</td>
<td>13 (5.3%)</td>
</tr>
</tbody>
</table>

ER endoscopic resection; HGIN high-grade intraepithelial neoplasia; LGIN low-grade intraepithelial neoplasia; IN intraepithelial neoplasia.

Interfering factors during procedure

Technical problems occurred during 2/243 MBM procedures (1% [95% CI 0-3%]). In one patient a 5Fr snare broke during the resection; the resection could be completed without further problems with a new 7Fr snare. In another patient the releasing wires got entangled around the pseudopolyp. After releasing all rubber bands the wires were freed and subsequently the resection could be performed.

Stenosis not allowing passage of the endoscope with the MBM cap was encountered in 6/243 MBM procedures (3% [95% CI 1-5%]). In 3 procedures the stenosis was resolved by dilatation prior to MBM in the same session, 2 procedures were postponed to allow dilatation and in 1 procedure simple snare resection was performed distal to the stenosis.

Clinically insignificant bleeding obscuring the endoscopic view and therefore requiring endoscopic hemostasis during the MBM-procedure was seen during 49/243 procedures (20% [95% CI 15-25%]). Hemostasis was achieved by focal coagulation of the bleeding vessel with the tip of the snare (32), APC (3), electrosurgical hemostatic forceps (1), clip (7), adrenaline (1) or a combination of these therapies (5). These bleedings were not considered acute complications but an intrinsic event to resection, since the management of the patient did not alter: none resulted in hospital admission, blood transfusion, or repeat endoscopic intervention and all were discharged after the normal post procedural observation period of 2 to 4 hours.

Complications

Acute complications (during procedure)

Although no lifting was used in any of the 243 procedures, none of the 1060 MBM resections resulted in a perforation (0% [95% CI 0-0.3%]) (Table 3).

Clinically significant bleeding occurred in 7/243 procedures (3% [95% CI 1-6%]). Hemostasis was achieved with standard endoscopic therapy during the procedure (tip of the snare in 4; clip in 1; clip and adrenaline in 1; APC and adrenaline 1). Six bleedings were graded as a ‘mild’ complication as these patients had an unplanned hospital admission and were discharged after
1-2 days of observation. One bleeding was graded as a ‘moderate’ complication as the patient underwent elective endoscopic re-inspection without additional intervention. None of the patients with a clinically significant bleeding during the MBM procedure developed a recurrent bleeding. Clinically significant bleeding was associated with a higher number of resections per procedure (p=0.02) with an odds ratio of 1.19 (95% CI 1.02-1.40) per resection.

Table 3. Acute plus early complications and endoscopic efficacy

<table>
<thead>
<tr>
<th></th>
<th>Number</th>
<th>Percentage</th>
<th>95% C.I.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acute complications</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perforation</td>
<td>0</td>
<td>0%</td>
<td>0% - 0.3%</td>
</tr>
<tr>
<td>Bleeding</td>
<td>6 ‘mild’</td>
<td>3%</td>
<td>1%-6%</td>
</tr>
<tr>
<td></td>
<td>1 ‘moderate’</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Early complications</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bleeding</td>
<td>5 ‘moderate’</td>
<td>2%</td>
<td>0.7% - 5%</td>
</tr>
<tr>
<td>Stenosis</td>
<td>24 ‘moderate’</td>
<td>48%</td>
<td>36% - 60%</td>
</tr>
<tr>
<td></td>
<td>9 ‘severe’</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Complete endoscopic resection</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Focal lesions</td>
<td>103</td>
<td>91%</td>
<td>84% - 96%</td>
</tr>
<tr>
<td>Delineated area</td>
<td>101</td>
<td>86%</td>
<td>80% - 93%</td>
</tr>
<tr>
<td>Escape treatment</td>
<td>13</td>
<td>100%</td>
<td>75% - 100%</td>
</tr>
</tbody>
</table>

C.I. confidence interval
A calculated per resection
B calculated per patient in the (stepwise) radical resection protocol

Early complications (within 30 days after procedure)
Early complications consisted of 5/243 delayed bleedings (2.1% [95% CI 0.7-4.7%]), 4 of these occurring within 48 hours and 1 after 6 days. All delayed bleedings were effectively managed endoscopically and graded as ‘moderate’ as a repeat endoscopy was required in all cases and blood transfusion with less than 4 units in 3 cases. No association was found between delayed bleeding and the number of specimens resected.

Symptomatic stenosis occurred in 33 patients and only after procedures that were part of the (stepwise) radical resection protocol (33/69 patients; 48% [95% CI 36-60%]). Stenosis was graded as ‘moderate’ in 24 patients (resolving after ≤5 dilatations) and ‘severe’ in 9 patients (as >5 dilatations, incision therapy or stent placement was necessary). No symptomatic stenoses occurred after procedures for focal ER of a lesion or after escape ER of remaining BE after RFA.

Mortality within 30 days occurred in 1 patient 24 days after the MBM procedure, however, this was not attributable to MBM procedure. The patient was admitted 18 days after MBM because of severe ischemia of the left leg (Fontaine stage IV) for which percutaneous transluminal angioplasty (PTA) was performed. The patient subsequently developed cardiopulmonary and renal insufficiency and died 6 days after admission.
Endoscopic efficacy

Focal lesions
Complete endoscopic resection of a delineated focal lesion was achieved in 103/113 procedures (91% [95% CI 84-96%]), including 3 procedures (3%) in which additional therapy with APC for remaining margins or bridges was used to achieve complete resection. All failures were due to scarring, impeding suction of the tissue into the cap. Scarring was attributed to prior ulceration (n=6) or prior ER (n=4).

Delineated area
Complete endoscopic resection of a delineated area as part of the (stepwise) radical resection protocol and as escape treatment after RFA was achieved in 101/117 (86% [95% CI 80-93%]), including 44 procedures (38%) in which additional therapy with APC for remaining margins, bridges or islands was used to achieve complete resection. Failures were due to scarring because of prior ulceration (n=4), prior ER (n=11) or both prior ulceration and ER (n=1).

Escape treatment
Complete endoscopic resection as escape treatment after radiofrequency ablation for remaining BE was achieved in 13/13 procedures (100% [95% CI 75-100%]). None of the procedures resulted in remaining margins or bridges.

Discussion
This is the largest prospective series demonstrating the safety and endoscopic efficacy of MBM in ER for BE. MBM in BE proved to be safe as no perforations occurred in over 1000 resections, with only 3% acute and 2% delayed bleeding. MBM also allowed for effective removal of the delineated target area in the vast majority of cases unless the area was scarred due to prior ulceration or endoscopic therapy.

No perforations occurred in 1060 resections with MBM despite the absence of submucosal lifting. No submucosal lifting was used as the rubber bands are thought not to be strong enough to hold the deeper muscle layer of the esophagus in case it is captured in the rubber band. The snare was placed below the rubber band since this is technically easier and ensures that the pseudopolyp can be resected in one piece. In contrast, closure of the snare above the rubber band may cause the snare to cut through the back-end side of the pseudopolyp, especially at the level of the
Part II: Endoscopic therapy in Barrett’s esophagus

cardia where the pseudopolyp may not be oriented perpendicular to the longitudinal axis of the esophagus. Perforations occur in approximately 1% of the endoscopic resections performed with the widely used ER-cap technique in the BE.[3,19] The chance of perforation with MBM seems to be extremely low in BE, although not impossible as perforation after MBM has already been described.[20]

The number of acute complications, i.e. complications occurring during the procedure, was low during MBM procedures: in our series only 3% of the procedures resulted in a clinical significant bleeding. This finding is in discordance with previous studies reporting acute bleeding rates of 30% during MBM in BE, and 23% with the ER-cap technique.[3,4] This discrepancy reflects differences in the definition of these studies. Most acute bleedings resolve spontaneously or can effectively be treated by coagulation with the tip of the snare. Analogous to surgery acute bleeding was only considered a clinically relevant complication if they led to unplanned admission, endoscopic re-intervention and/or need for blood-transfusion.

Early complications occurring within 30 days after the procedure consisted of delayed bleedings and stenoses. The rate of delayed bleeding was again low: 2%. This is similar to the reported rate of 1% delayed bleeding after ER-cap and other ligate-cut ER techniques.[2,3] All delayed bleedings occurred within a week after the procedure, were easily treated with endoscopic hemostatic therapy and three patients required blood transfusion.

Stenosis requiring dilatation developed in 48% of the patients who underwent the MBM procedure as part of the (stepwise) radical resection protocol. This is in accordance with other studies that have reported stenosis rates of 26-70% after radical resection of the whole Barrett’s segment.[4,7,21,22] Stenosis rate increases with the extent of the resected area in the esophagus, especially if the resection is longer than 3 cm in length and comprises more than 75% of the circumference.[23] Our data do not allow evaluating if MBM is associated with a higher rate of stenosis than the ER-cap procedure.

Complete endoscopic resection was high: in 91% of delineated focal lesions, in 86% of delineated areas in BE and in 100% of the escape treatments. This is similar to the 88% success rate reported for complete endoscopic resection after ER-cap.[19] The main cause of failure with MBM was fibrosis and scar formation which impeded suctioning of the mucosa into the cap and subsequent rubber band ligation. Probably other resection techniques would have failed as well in these fibrotic areas.

There are some limitations that need to be addressed. First, this study was performed in tertiary centers with specialized endoscopists with extensive experience with other endoscopic resection techniques. The experience of these endoscopists may have favored the safety and efficacy of MBM. Also a selection bias of more simple cases may have occurred as several ER techniques were
available at the same time and endoscopists had no restrictions when choosing the ER technique. Second, in this study MBM only has been evaluated in BE, therefore the safety of MBM in other parts of the GI-tract is unknown, like in for example the duodenum which has a considerably thinner wall. Finally, MBM was not compared to other endoscopic resection techniques, especially the widely used ER-cap technique. As a result, a comparison of safety and efficacy with other resection techniques cannot be made from our data. On the other hand, MBM seems to have more advantages as it is faster and cheaper than the cap technique for piecemeal resections.\cite{24}

This study demonstrates that MBM is a safe and useful tool for ER in BE by experienced endoscopists. Although the technique itself is easy to learn, we believe that MBM should only be performed in centers with experience with imaging and therapy of BE for several reasons. First, it is essential to recognize the subtle abnormalities that may harbor cancer and need to be resected. Adequate imaging and recognition is also necessary for complete endoscopic resection in one procedure as a repeat resection later on is considerably more difficult and less effective. Second, although complication rates are low, endoscopists should be able to treat all possible complications. Third, proper pathological assessment of ER specimen is essential for further patient management. Finally, treating physicians should be familiar with other, additional or complementary techniques in endoscopic therapy for Barrett's neoplasia, such as RFA, in order to be able to offer a complete endoscopic treatment algorithm to patients with neoplasia in BE.

In conclusion, in this largest prospective series of MBM in BE, we showed that MBM is safe and effective. Despite the absence of submucosal lifting, perforations did not occur. Only a small number of MBM procedures resulted in bleeding, which could all be managed endoscopically and MBM allowed for effective removal of the delineated target area in the vast majority of cases.
Part II: Endoscopic therapy in Barrett’s esophagus

References


