Advances in endoscopic resection and radiofrequency ablation of early esophageal neoplasia
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Do’s and don’ts of endoscopic resection: lessons learned from a structured training program

**ABSTRACT**

**Background:** Endoscopic resection (ER) is the cornerstone of endoscopic management of esophageal high-grade dysplasia or early cancer. However, ER is a complex technique requiring knowledge and expertise. **Aims:** To identify the most important learning points in performing ER in a training setting and to provide information on how to improve ER technique.

**Methods:** Six gastroenterologists at centers with multidisciplinary expertise in upper GI oncology participated in a structured ER training program, consisting of 4 mutual training days with lectures and hands-on training on live pigs, at least 4 one-on-one hands-on training days, and written feedback on video recordings of ER procedures by an highly experienced endoscopist in ER. The first 20 ERs of each participant (total 120 ERs) were prospectively registered. Learning points as experienced by the participating endoscopists were assessed using a questionnaire, and by review of written feedback reports of 33 video recordings of unsupervised ERs. Three endoscopists with experience in ER selected the most important learning points.

**Results:** The most important learning points were: to ensure and optimize the endoscopic view by choosing the best available endoscope and cleaning of the area of interest; rotate the endoscope to position the lesion at 6 o’clock; delineate the lesion by placing electrocoagulation markers thus creating a ‘preprocedural plan’; perform a test-suction prior to every resection to avoid too much overlap or residual tissue bridges.

**Conclusions:** This study assessed and summarized the most important learning points in performing ER that were encountered during a structured ER training program.
INTRODUCTION

Endoscopic resection (ER) is considered the cornerstone of endoscopic management of high-grade dysplasia (HGD) and early cancer (EC) in the esophagus. Endoscopic resection (ER) not only removes the visible lesion, but also provides a specimen for histological assessment and staging. This allows for selection of suitable candidates for subsequent endoscopic treatment, and defines which patients should be referred for surgery because of an increased risk for lymph node involvement. Several studies have shown that ER is safe and effective for the removal of focal early neoplastic lesions in Barrett’s esophagus as well as for early esophageal squamous neoplasia.\textsuperscript{1,2,3-7}

Endoscopic treatment of early neoplasia in the upper GI-tract is becoming more accepted in the GI-community, because an increasing number of studies have shown that endoscopic treatment of early neoplastic lesions is safe and effective.\textsuperscript{1,2,3-10} In addition, we expect an increase in the number of detected early neoplastic lesions due to ongoing developments in endoscopic imaging techniques, and screening and surveillance programs. Furthermore, the newest generation of endoscopic treatment modalities, such as ER with multiband mucosectomy (MBM), is easy-in-use, making endoscopic treatment more attractive to a wider range of endoscopists. Therefore, we anticipate that endoscopic treatment may become more widely available in expert centers and non-expert centers.

ER, however, is a technically demanding procedure that requires knowledge and expertise to ensure complete removal of the lesion, to avoid complications such as perforation, and to manage intra-procedural bleedings that occur in 20-25\% of cases. Endoscopists who perform ER should therefore be trained in the technicalities of the procedure and the prevention and management of complications.\textsuperscript{5,6,11} We therefore developed a structured ER training program to implement ER in a safe and controlled manner in the Netherlands. In this training program, six endoscopists from selected centers were trained in ER, and all procedures and complications were registered prospectively to assess the safety and efficacy of ER in a training setting and to identify potential learning curve effects. The clinical results of this study have been published elsewhere.\textsuperscript{12} During the ER training program, numerous learning points, mistakes and difficulties of ER were identified, that may be highly informative for endoscopists who perform ER or are training in ER. The aim of the current study was to identify important learning points in ER as assessed by expert endoscopists, and pointed out by the participating endoscopists in the ER training program, using a questionnaire. Based on the learning points that were identified, we aimed to provide practical recommendations for improvements in ER skills.

METHODS

The ER training program

The organizational background of this study was the Dutch ER training program. The aim of the ER training program was to implement ER in the Netherlands, including the proper endoscopic work-up and the histological assessment of ER specimens in accordance with
national guidelines. Other objectives of the ER training program were: 1) to improve the quality of endoscopic detection and treatment of early neoplastic lesions and the histological assessment of ER specimens; 2) to implement prospective registration of procedures and complications and mutual treatment protocols; 3) to build a platform for scientific research and guideline development. The training program was organized by the Academic Medical Center, Amsterdam, by a committee of two endoscopists, two pathologists, two endoscopy nurses, two research fellows, and a research nurse, all with extensive experience in the field of endoscopic treatment of early esophageal neoplasia. The ER training program was funded by the organizing center (33%), participating centers (33%), and sponsors (33%).

Participants of the training program were selected to fit the following profile: they all were fulltime gastroenterologists in a large regional or academic center with established multidisciplinary expertise in oncology of the upper GI tract (high volume center for upper GI-surgery, availability of EUS, histopathological expertise, and facilities for radiotherapy and oncology care). Endoscopists participated in the training program together with an endoscopy nurse and a pathologist of their own center.

The training program consisted of four one-day training days with three-months-interval comprising theoretical lectures, live demonstrations, and hands-on training on anaesthetized pigs under guidance of international expert endoscopists and pathologists. Additionally, individual hands-on training days were scheduled at the participant’s center and at the training site on which 6-8 ER cases were scheduled for one-on-one training of the endoscopist and endoscopy nurse by the trainers. During the training program, ER was performed with the ER-cap technique or the MBM-technique as previously described in detail. Participating endoscopists were encouraged to make digital video recordings of the first (non-supervised) 10-20 ER procedures performed at their own center. Video recordings were reviewed by an expert endoscopist (JB) of the organizing committee, resulting in a written feedback report. In addition, ER specimens of the first 10-20 ER procedures performed at the participants’ own center were reviewed by a pathologist with extensive experience in ER (FtK or MV) at the training site.

Data collection
All ER procedures performed during the ER training program were prospectively registered, using standardized case registration forms for procedure characteristics and complications (www.endosurgery.eu). Learning points in performing ER were collected from two different sources: 1) written feedback reports of video recordings from the first non-supervised 10-20 ER procedures per endoscopist that were reviewed by an expert endoscopist (JB) of the organizing committee, 2) a questionnaire, sent to the six participating endoscopists, after all had performed at least 20 ER procedures. Endoscopists were asked to describe a maximum of three learning points for the following items: work-up and imaging; marking of the lesion; submucosal fluid injection and suctioning of the lesion in the cap; resection; MBM technique; ER-cap technique; retrieval of the specimens; complications; and, miscellaneous.
Outcome measures
The most important learning points in performing ER were selected from these two sources in a consensus meeting of three experienced endoscopists in ER (qualitative evaluation). ‘Important’ was defined as having influence on the efficacy, safety, or practicality of ER.

Data collection and statistics
The SPSS statistical software package (SPSS Inc., Chicago, IL, USA) was used for data analysis. For descriptive statistics, mean (±SD) was used for normal distribution and median (IQR or range) was used in case of skewed distribution.

RESULTS

ER training program and participants
Six teams consisting of an endoscopist, endoscopy nurse and pathologist attended all four training days. In addition, participating endoscopists had a median of 5 (IQR 2-7) one-on-one hands-on training days, supervised by an expert endoscopist. Fifty-five of 120 ER procedures (43.3%) were supervised by an expert endoscopist. A median of 4 (IQR 2-6) video recordings of non-supervised ER procedures per endoscopist were reviewed and commented by a single expert endoscopist of the training program committee, resulting in a total of 33 written feedback reports. All six endoscopists completed the questionnaire on learning points in performing ER.12

ER procedures
Of 120 consecutive esophageal ER procedures, 109 were performed in Barrett's esophagus and 11 for squamous neoplasia, including 85 piecemeal ERs (median of 3 (IQR 2-4) specimens). Details on the ER procedures have been described elsewhere in detail.12 In summary, the ER-cap technique was used in 85 procedures and the MBM technique in 35 procedures (Figure 1; Figure 2). Complete endoscopic removal was achieved in 111/120 (91.6%) cases (Figure 3). Acute complications were 6 perforations (5.0%): 5 were effectively treated endoscopically (clips, covered stent); 1 patient underwent esophagectomy the same day. Four perforations occurred during a non-supervised

Figure 1: Endoscopic resection (ER) using the ER-cap technique. A: submucosal lifting; B: suctioning of the lesion in the cap, with the resection snare placed in the rim of the cap; C: closure of the snare during suctioning; D: resection wound after using coagulation to cut of the pseudopolyp, resulting in removal of the lesion.
procedure of which three perforations were recorded on video. Eleven intraprocedural bleedings (9.2%) were managed endoscopically.

**Outcome measures: learning points in endoscopic resection**

Learning points derived from the questionnaire completed by the six participating endoscopists, and from the written feedback reports of ER video recordings were assessed. The most important learning points as judged by the three experienced endoscopists are described in detail below together with corresponding technical recommendations.

**Work-up and imaging**

- Optimize the endoscopic view: at the start of the ER procedure the endoscopist should empty the stomach and clean the target area in the esophagus by flushing with water to remove mucus and gastric contents. During the procedure, systematic emptying of the stomach and esophagus should be repeated frequently. This ensures an optimal overview of the working area and prevents aspiration during the endoscopy. It is advisable to use antifoam either orally administered to the patient prior to the endoscopy or in the water used for flushing.
- Use an endoscope with a separate water jet channel: to enable simultaneous flushing of water and interventions through the working channel of the endoscope for optimal overview when bleeding occurs.
Do’s and don’ts of endoscopic resection

- Do not compromise detection and delineation: most therapeutic gastroscopes have an inferior image quality compared to their diagnostic counterparts. In case it is difficult to detect and delineate the lesion prior to ER, optimize inspection by using a high-resolution endoscope supplemented with (virtual) chromoendoscopy techniques.

- Retroflex for lesions located at the cardia (Figure 4): perform inspection with the endoscope in the retroflexed position with adequate inflation of air. This orientation significantly improves the visualization of the distal margin of lesions and improves the practicality of delineation and submucosal lifting (see below). Use a flexible endoscope that can easily make the U-turn into the retroflexed position.

- Insufflate sufficient air: insufflate air until there is a good overview in the esophagus. In case it is difficult to insufflate the esophagus, the patient may be sedated too deeply.

- Use the Paris classification: description of the macroscopic type of the lesion may contribute to more thorough inspection of the lesion and helps the endoscopist in recognition of early neoplastic lesions.\(^\text{15}\)

Figure 4: Retroflex for lesions located at the gastric cardia, to improve the visualization of the distal margin of lesion and improve the practicality of delineation and submucosal lifting prior to ER. A/B: patient 1: early neoplastic lesion in Barrett’s esophagus at 10 o’clock at the cardia, antegrade view (A) en retrograde view (B); C/D: patient 2: early neoplastic lesion in Barrett’s esophagus at 11 o’clock at the cardia, antegrade view (C) and retrograde view (D).

Delineation and marking of the lesion

- Place electrocoagulation markings to delineate the area to be resected (Figure 5). This ‘pre-procedural plan’ should be adhered to during the remainder of the procedure. During the procedure the overview on the working area will diminish due to visualization through the ER-cap, the use of submucosal lifting, bleeding or electrocoagulation effects. The endoscopist may then loose the orientation and perspective on the lesion causing incomplete or unnecessarily large resections. A ‘pre-procedural’ plan created under optimal imaging circumstances prior to the resection is a roadmap for an effective and safe ER.
Place the electrocoagulation markings (tip of the snare of argon plasma coagulation (APC)) with a 2-5 mm distance from the lesion. For lesions in the distal esophagus or cardia, markers can best be placed with the endoscope in the retroflexed position.

Obtain a still image of the marked lesion to assess if delineation and markings are adequate. Some of the markings may be more important than others; e.g. since they are close to the edge of the lesion.

In case of doubt if all markings and the complete lesion are removed perform an additional ER of that site. Subsequent ER at a later stage will be significantly more difficult due to scarring.

Submucosal fluid injection in ER-cap and suctioning of the lesion in the cap

- Start to inject fluid through the injection needle just before the needle traverses the mucosa. Perform the fluid injection in a stepwise manner to be able to assess the effect of the lifting and avoid too much lifting of the mucosa outside the delineated area since this only obscures the view of the working area.
- In case of piecemeal ER, lift the edges of the previous ER prior to subsequent resections to avoid perforation. In case of residual bridges, lift the tissue bridge and the ER wound before resection.
- Lift an area with fibrosis or scarring first; otherwise only surrounding tissue will lift which will obscure the view of the area of interest. In case of a poor lifting: do not perform ER of these areas (Kato lifting classification).16
- Perform a ‘test suction’ prior to the endoscopic resection to evaluate how much and which part of the lesion enters the cap. The test suction is performed before placement of the ER-snare in the ridge of the cap (for ER-cap procedures) or before releasing a rubber band (for MBM procedures). The endoscopist may adjust the position of the cap, the pressure of the cap onto the tissue, the amount of suction, and the way the cap is maneuvered during suctioning of the tissue. A test suction is also important to judge if the amount of overlap between two ERs is not too large (increases perforation risk) or too small (results in remaining tissue bridges between adjacent resections).
Do’s and don’ts of endoscopic resection

**Apply controlled suctioning**: evaluate the suction force during the test suction and prior to resection. Control the suctioning force with the suction button or by creating an air leak between the cap and the esophageal wall during suctioning (reduces the suction force). Having control over the suction force is especially helpful when a smaller sized resection is intended.

**Resection**

- Keep the vacuum on the resection cap until the snare is completely closed (for ER-cap procedures) or the rubber band is released (for MBM procedures): in case the vacuum is released too fast, only a superficial resection of a small specimen achieved is performed, with a higher risk for non-radical resection at the vertical margin.
- In case the tissue lacerates while entering the cap during suctioning: continue the suction and resect the lesion. There is no increased perforation risk since the laceration occurs at the level of the mucosal layer. Do not stop to reinspect: bleeding will impair visualization. Provided that the lesion has been adequately lifted: continue suctioning and perform resection according to your pre-procedural plan and prior test suction.
- After resection, immediately inspect the ER wound to exclude perforation and bleeding, and to assess the completeness of the resection. Store the ER specimen in the stomach: separate removal of each specimen after resection is time consuming, introduces a delay in case of bleeding, and generally does not contribute to clinical management since piecemeal resections do not allow reliable reconstruction of the resected lesion (at least not in Barrett’s lesions).
- For lesions in the cardia or distal esophagus: inspect, delineate and inject the distal margin in the retroflexed position. Suctioning the lesion in the cap and the actual resection, however, should be performed in the antegrade position.

**Multiband mucosectomy technique**

- Optimize the endoscopic view (Figure 6): 1) align the pulling strings of the MBM-barrel with the working channel to keep them out of the endoscopic view (prior insertion of the endoscope), 2) in case only 1-3 resections are required (the majority of cases): release 2-3 rubber bands prior to introducing the endoscope since this greatly improves visualization.
- During the endoscopic resection with the MBM technique close the snare quicker and more forcefully while cutting through the specimen. Compared to the ER-cap technique the MBM technique may be more prone to coagulation trauma because the snare is thicker and no submucosal lifting is performed.

**ER-cap technique**

- Position the lesion at the 6 o’clock position in the endoscopic view (Figure 7). Most ER-cap procedures are performed with an oblique cap with the shorter part of the cap orientated at the 6 o’clock position and the longer part at 12 o’clock. With this orientation it is imperative that the endoscope is rotated in such a way that the lesion is positioned at the 6 o’clock position. This holds especially during the suctioning of the
If the lesion is located at the 12 o’clock position closure of the snare will result in dislocation of the snare from the ridge of the cap and tangential cutting through the specimen. In addition, the 12 o’clock position will result in a higher pressure on the esophageal wall with less effective suctioning. Both effects may result in a small sized specimen with a higher chance of non-radical vertical resection margin.

Position the snare in the rim of the cap in such a way that the two wires are located at the lower half of the endoscopic view at the location of the working channel of the endoscope. This ensures that during closure of the snare the base is captured of the tissue that is suctioned in to the cap. If the wires are located at the 12 o’clock position closure of the snare will result in dislocation of the snare from the rim of the cap. The snare will then not capture the base of the pseudopolyp but close halfway through.

**Figure 6:** Optimize the endoscopic view using the multiband mucosectomy (MBM) technique. **A/B:** by aligning the pulling strings of the MBM-barrel with the working channel to keep them out of the endoscopic view prior insertion of the endoscope; **C/D:** by releasing 2-3 rubber bands prior to introducing the endoscope (in case only 1-3 resections are required).

**Figure 7:** Positioning of the lesion during endoscopic resection using the oblique cap. **A:** lesion in the esophagus; **B:** Incorrect: a 12 o’clock position requires an angulated position of the endoscope to suction the lesion in the cap. In such a position suctioning may be less effective due to the higher tension on the esophageal wall and the snare will not close at the base of the lesion. This may result in a more partial/superficial resection of the lesion; **C:** Correct: rotate the endoscope to place the lesion at the 6 o’clock position in the endoscopic view for injection, suctioning and resection.
Do’s and don’ts of endoscopic resection

- Prevent dislocation of the snare from the rim of the ER-cap. Placement of the snare in the rim of the cap is not easy. Subsequent approach of the target area, correct positioning of the cap onto the lesion, suctioning of the tissue, closure of the snare, and resection have to be well coordinated between endoscopist and endoscopy nurse. This is a delicate process and manipulations of the cap onto the lesion or changes of scope position may result in dislocation of the snare from the rim of the cap. Therefore a prior test suction enables the endoscopist to target the resection area in a more straightforward manner.

- A new snare should be used for every ER-cap resection. The crescent shaped ER-snares are very thin and generally lose their shape during the forceful closure of the resection process. Opening and repositioning of the snare in the rim of the cap for an additional resection is generally not possible. This in contrast to the MBM technique where the hexagonal snare of the MBM kit can be used for multiple resections.

- Do not use the large flexible ER-cap for piecemeal ER, because this may carry a higher perforation risk.

Retrieval and handling of specimens

- Store the ER specimens in the stomach and use a retrieval net at the end of the procedure. Never remove two specimens in the cap, because the most distal ER specimen may not be suctioned vacuum in the cap, and may fall in the trachea. Use a filter in the suctioning system, for the case that a minute specimen is suctioned away through the suction channel of the endoscope.

- Pin down the specimens on cork or paraffin to optimize orientation and cutting in the pathology lab. Avoid inwards curling of the lateral edges since positive lateral margins (not uncommon in piecemeal resections) may then give the false impression of a non-radical deep resection margin.

Complications

- Management of bleedings: slowly move the edge of the transparent cap over the esophageal wall to localize the bleeding focus and to gently compress the bleeding site to achieve hemostasis. Wait to see if the bleeding is stops spontaneously, while keeping the bleeding in the endoscopic view. Flush with little boosts of water using a water jet system but avoid prolonged flushing. If the bleeding is not self-limiting, apply coagulation with the tip of the snare. This should be done with minimal pressure on to bleeding site to avoid deep damage. In case this does not result in hemostasis, use a hot biopsy forceps. Placing clips is not preferred as an initial measure since the clip generally complicates further piecemeal resections.

- Management of perforations: in case perforation occurs during ER do not insufflate air, but switch to CO2-insufflation, place a sump tube at the perforation site, and start antibiotics. There are two key questions that guide further management. First, can the neoplasia still be effectively treated endoscopically? It makes little sense to manage a perforation conservatively and/or endoscopically if final management of neoplasia (e.g. because of a submucosal invading cancer) will require esophagectomy.
anyway. Second, is effective closure of the perforation feasible without compromising the success of treating the neoplasia? New clipping devices may effectively close large perforations but may also bury residual neoplasia at the perforation site. Covered stents may effectively seal the perforation site and are especially effective is there is local narrowing of the esophagus preventing dislocation.

Miscellaneous

- Fix the resection cap to the tip of the endoscope with a strap of tape. This prevents the cap slipping off when there is a resistance e.g. at the upper esophageal sphincter or at the level of an esophageal stenosis. Check if the cap-size is suitable for the diameter of the endoscope.
- Instrumentation: keep the instruments (e.g. snare, APC-probe, injection needle) close to the tip of the endoscope for better control.

DISCUSSION

In this study, the lessons in ER technique learned from a training program in ER were assessed. Learning points as experienced by the participating endoscopists or observed by the training program committee during the evaluation of video recordings were listed. Subsequently, the most important items, with an impact on the safety and efficacy of ER, were selected by three expert endoscopists and discussed in detail. This resulted in a useful summary of ‘Do’s and Don’ts in ER’, which may be valuable for endoscopists with an interest in learning or improving ER technique.

A limitation of this study is that participating endoscopists in the ER training program were strongly influenced by the expert opinion of the endoscopists of the ER training committee who acted as trainers. This is illustrated by an overlap of learning points derived from the questionnaire and the feedback reports. Therefore, we have not performed a quantitative analysis of the learning points. We believe that a qualitative analysis of the learning points by three expert endoscopists would be a more accurate way to select the most important items. We realize that this study is partly based on expert opinion yet we feel that it provides practical tips on ER technique.

The results of the ER training program suggest that structured ER training is of great value: numerous learning points were identified, and all complications were adequately managed. Details on the clinical outcome have recently been published elsewhere. The most important finding was that the ER training program resulted in a relatively high perforation rate of 5%. Review of video fragments revealed circumstances that may have contributed to the occurrence of perforation, such as poor visibility, suboptimal lifting of the target area and uncontrolled suctioning of small residual tissue bridges. This suggests that some factors related to perforation may be operator-dependent, which is an argument to continue ER training for endoscopists and their team. In addition, the extended list of learning points derived from the questionnaire that was sent to the participating endoscopists reflects their expanded knowledge on ER. Finally, the ER
training program committee observed that the teams of endoscopist, endoscopy nurse and pathologist greatly improved their skills, understanding, and confidence in the detection and delineation of lesions, selection of patients, ER technique, and management of complications. We therefore argue that ER training is effective and advocate that, to optimize ER treatment and to ensure adequate management of complications of ER, ER should be performed by trained endoscopists in centers with multidisciplinary experience with ER.
REFERENCES


