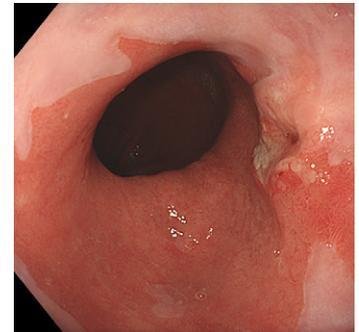


Mistakes in endoscopic treatment of Barrett oesophagus neoplasia and how to avoid them

Eva P.D. Verheij, Roos E. Pouw and Jacques J. Bergman

Barrett's oesophagus is a premalignant condition of the distal oesophagus predisposing to oesophageal adenocarcinoma. Given the potential for malignant progression and the poor prognosis of oesophageal adenocarcinoma when diagnosed at a symptomatic stage, patients with known Barrett oesophagus undergo regular endoscopic surveillance to detect neoplastic progression at an early and preferably endoscopically, treatable stage. Endoscopic management of early Barrett oesophagus neoplasia consists of a combination of endoscopic imaging, endoscopic resection and endoscopic ablation. Below we discuss a number of mistakes that are frequently made when managing Barrett oesophagus neoplasia and how to avoid them. Much of this discussion draws on existing guidelines (for background reading, check the ESGE Barrett oesophagus guideline¹), but in many instances the underlying evidence (even in the guideline) is missing and therefore many of our practically driven recommendations are based on common sense and our experience in this field.



Mistake 1 Spending insufficient time cleaning and inspecting the Barrett segment during endoscopic surveillance

With inadequate cleaning and immediately 'jumping' to obtain the inevitable random biopsy samples there is no chance that you will detect the more subtle Barrett lesions. So, please spend a couple of minutes to optimize imaging, as this will dramatically increase your chances of detecting relevant disease.

Use the waterjet of your endoscope to clean the Barrett segment—this generally takes 1–2 minutes. If you wonder whether you have cleaned the segment well enough, then it is generally not 'just right' yet. Switch to optical chromoscopy: if the oesophagus looks impeccably clean on narrow-band imaging (NBI), then your cleaning is optimal (figure 1).

Subsequently, you should spend 3–5 minutes inspecting the segment using white light endoscopy. Switching back-and-forth with optical chromoscopy, which will create a different perspective, will help you to see more. Retroflex the endoscope to inspect the 'danger zone'—the area where the Barrett segment transits into the hiatal hernia (figures 2 and 3). This is the area that has the highest risk of neoplasia and the highest risk of neoplasia being missed endoscopically. Look longer, biopsy less! After taking your first biopsy sample most of your imaging opportunities are lost.

Finally, know the face of Barrett oesophagus neoplasia (figure 2). Detecting early neoplasia is all about recognizing how early neoplasia

actually looks. Excellent training modules are available for this at BEST Academia [www.best-academia.eu].

Mistake 2 Trusting a pathology report more than your own eyes

You should not automatically be reassured if a biopsy sample taken from a visible abnormality

in a Barrett oesophagus segment is diagnosed as non-dysplastic or inflammatory. In reality, this situation requires either endoscopic resection of the abnormality for optimal diagnosis or repeat endoscopy to document its regression, because a lesion that clearly looks neoplastic on endoscopy generally is neoplastic. Keep in mind that it is also not impossible for biopsy samples to be misplaced and that the histological assessment might not

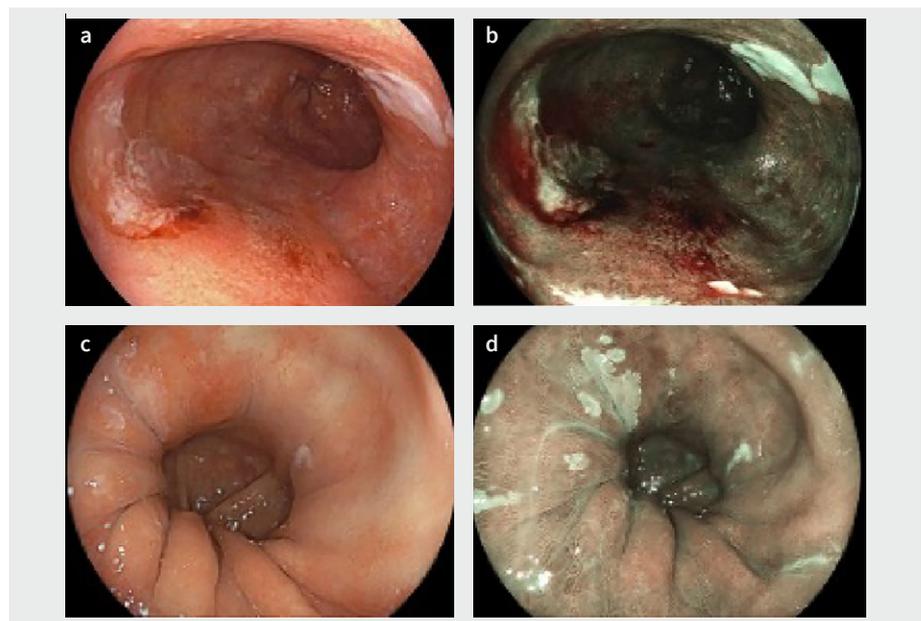


Figure 1 | Cleaning of the Barrett oesophagus segment to optimize imaging. **a** and **b** | An inadequately cleaned Barrett segment as seen on white light endoscopy and narrow-band imaging. **c** and **d** | An optimally cleaned Barrett segment as seen on white light endoscopy and narrow-band imaging. Endoscopic images courtesy of BEST Academia [www.best-academia.eu].

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Cite this article as: Verheij EPD, Pouw RE and Bergman JJ Mistakes in endoscopic treatment of Barrett oesophagus neoplasia and how to avoid them. *UEG Education* 2021; 21: 35–39.

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Images: courtesy of J.J. Bergman and BEST Academia.

Illustrations: J. Shadwell.

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Conflicts of interest: The authors declare there are no conflicts of interest in relation to this article.

Published online: December 20, 2021.

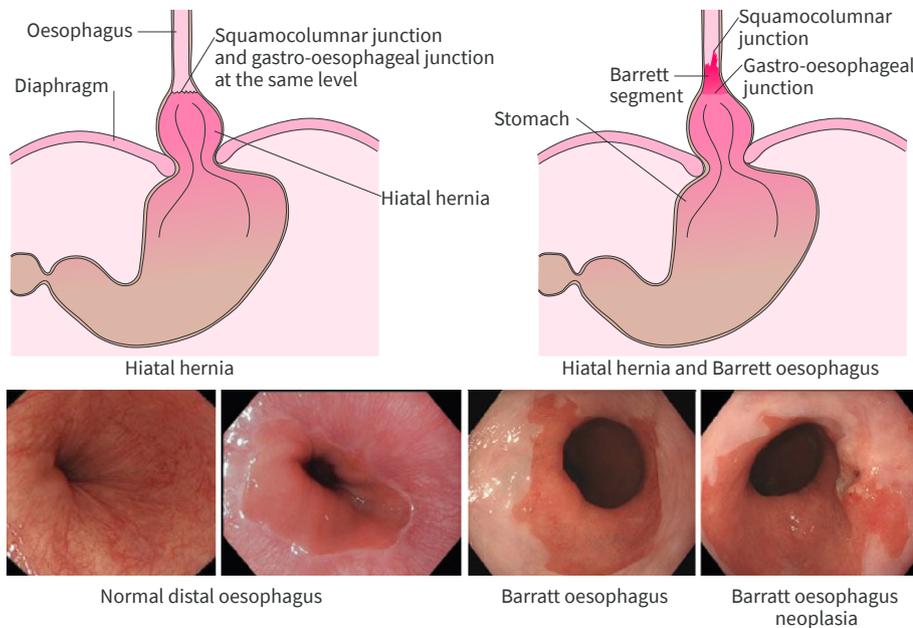


Figure 2 | The anatomy and appearance of Barrett oesophagus. Endoscopic images courtesy of BEST Academia [www.best-academia.eu].

Mistake 4 Ablating instead of resecting visible Barrett oesophagus lesions

The most common reason for neoplastic progression under ablation therapy is that at one of the ablation sessions a lesion has been ablated whereas it should have been resected (figure 4a and b). If you don't recognize visible lesions prior to ablation therapy, you run the risk of significantly delaying their diagnosis. If these lesions are ablated instead of resected, the first opportunity to pick them up is when the patient returns for the 3-month follow-up endoscopy.

For this reason, the endoscopist performing ablation therapy in patients with Barrett oesophagus should be able to switch gears to endoscopic resection. Indeed, ablation shouldn't be used as an excuse for not having to do an endoscopic resection. If you have not yet mastered the skills necessary to perform endoscopic resection then it is vital that you do so before embarking on endoscopic ablation in Barrett oesophagus.

Mistake 5 Ablating inflamed or swollen Barrett oesophagus mucosa

Ablation sessions are generally scheduled at 3-month intervals. In the majority of cases, this time is sufficient for the oesophagus to have healed after the prior ablation, provided the patient has received adequate acid suppression therapy. However, there is a subgroup of patients with delayed healing who will have a swollen, oedematous, Barrett oesophagus segment with exudates after the 3-month interval (figure 5). Please do not proceed with ablation in these cases. Prolong the interval between the ablation sessions instead and check the adequacy of your acid suppressant therapy.

If the Barrett oesophagus segment is inflamed then ablation will not be effective, given the thickness of the epithelium and the likely inadequate acid suppression. In addition, you run the risk of prolonging the period in which you will not be able to adequately inspect the segment for neoplastic progression. Continuing multiple 3-monthly cycles of ablation followed by poor healing will not allow you to detect neoplastic progression, especially when you have overlooked a visible lesion at the initial ablation.

Mistake 6 Starting the resection without marking the lesion

It is important to have a 'pre-resection plan' prior to embarking on the actual resection. The outer margins of your neoplastic target area may not be sufficiently visible once the multiband mucosectomy (MBM) kit has been assembled. In addition, resections and bleeding may hamper visualisation during piecemeal

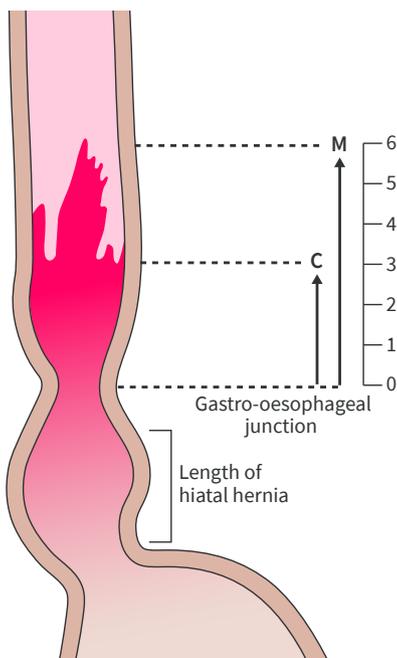


Figure 3 | Classification of Barrett oesophagus The Prague C + M criteria grade endoscopic Barrett oesophagus by defining the maximal length of circumferential columnar epithelium (C) and the maximal extent of columnar epithelium (M) proximal to the true position of the gastro-oesophageal junction. For example, C3M6 represents circumferential columnar epithelium of 3 cm and a maximal extent of columnar epithelium of 6 cm.

always be accurate. Communication with your pathologist on what you have biopsied is imperative for targeted biopsy samples. If your level of suspicion is high, please let your pathologist know. If you are uncertain whether your target lesion is inflammatory and your level of suspicion is low (e.g. when you have biopsied

close to the squamocolumnar junction in the presence of a grade A or B reflux oesophagitis), please provide this information as well.

Mistake 3 Performing therapeutic procedures without optimizing endoscopic imaging

We prefer to use a diagnostic endoscope for most therapeutic work in patients with Barrett oesophagus. Optimal imaging allows you to make the right decision regarding resection versus ablation and it allows optimal delineation of lesions. As already mentioned, the availability of a waterjet is essential to ensure adequate cleaning of the Barrett oesophagus segment.

During endoscopic resection, deal with bleeding before proceeding with your endoscopic submucosal dissection (ESD) or piecemeal resection. For piecemeal resections, any bleeding from prior resections must be adequately treated and the surface cleaned of blood and mucus. This also means that you should have emptied the stomach of fluids and blood before you embark on your next resection. If this stage is omitted, the stomach contents will reflux into the oesophagus while you are performing your next resection and may complicate matters if your next resection results in a bleed.

Be meticulously systematic at this stage: the time spent on optimizing imaging and the circumstances prior to resection always pays off in the end. In order to retrieve your specimens from the stomach at the end of the procedure you will need to empty the stomach of fluids anyway, so why not do this during the procedure to improve safety and efficacy of your resections?

procedures. Marking the target area with electrocautery markings before you begin the resection itself means you will have a roadmap to guide you through the remaining procedure and prevent you from getting lost in less-than-optimal imaging circumstances present during the MBM procedure (figure 4c–h).

Given the importance of marking, we generally use a diagnostic endoscope with a small distant attachment cap for this purpose. The cap allows us to stabilize the endoscope tip onto the mucosa during the marking. The use of optical chromoscopy and a near-focus mode (with Olympus endoscopes) or zoom function

(with Fujifilm or Pentax endoscopes) enables both the detection of the demarcation line and the controlled positioning of the electrocoagulation markers with the tip of the snare (for MBM procedures) or the ESD knife (figure 4i–n).

Mistake 7 Being ignorant about when to resect a lesion or choosing the wrong resection technique

Most of the early neoplastic lesions in Barrett oesophagus can be effectively removed by MBM. However, there is a subgroup of lesions that should not be resected by MBM because of the likelihood that there is deep submucosal invasion and/or a large intraluminal extent of the lesion. It is vital that endoscopists refrain from attempting MBM or endoscopic mucosal resection (EMR) for such lesions since it bound for failure and complications, and it compromises any subsequent endoscopic resection being performed by more experienced endoscopists. In case of doubt, obtain images and consult a more experienced colleague for their advice.

Mistake 8 Performing therapeutic interventions with inadequate training and an insufficient case load

All guidelines state that adequate training and a yearly case volume of at least 10 new patients with high-grade dysplasia or early cancer are needed for an endoscopist to be allowed to embark on treating new patients. To ensure these guidelines are met, therapy for Barrett oesophagus needs to be centralized. For instance, in the Netherlands all endoscopic ablations and resections performed in patients with Barrett oesophagus are centralized to eight centres—not one ablation or resection is performed outside these centres. As a result, the outcomes are clearly superior to those in geographic areas where treatment is not centralized.^{2,3}

Mistake 9 Being unprepared to manage significant bleeds

Most ESD bleeds can be managed by directing therapy to the vessel that has been accidentally cut. Coagulation forceps will do the job here. After MBM procedures, where the resection is ‘blind’ and less controlled than in ESD, the bleeding source may be more difficult to determine.

There are a few general rules when managing MBM bleeds. Do not remove the MBM cap unless it is absolutely necessary, because most bleeds can be treated by touching the bleeding site with the tip of the snare. Isolate the bleeding site by interrogating the resection site through the cap—you can use the edge or lateral side of the cap to compress the bleeding side. Finally, once you have identified the bleeding side only apply very gentle pressure with the tip of the snare.

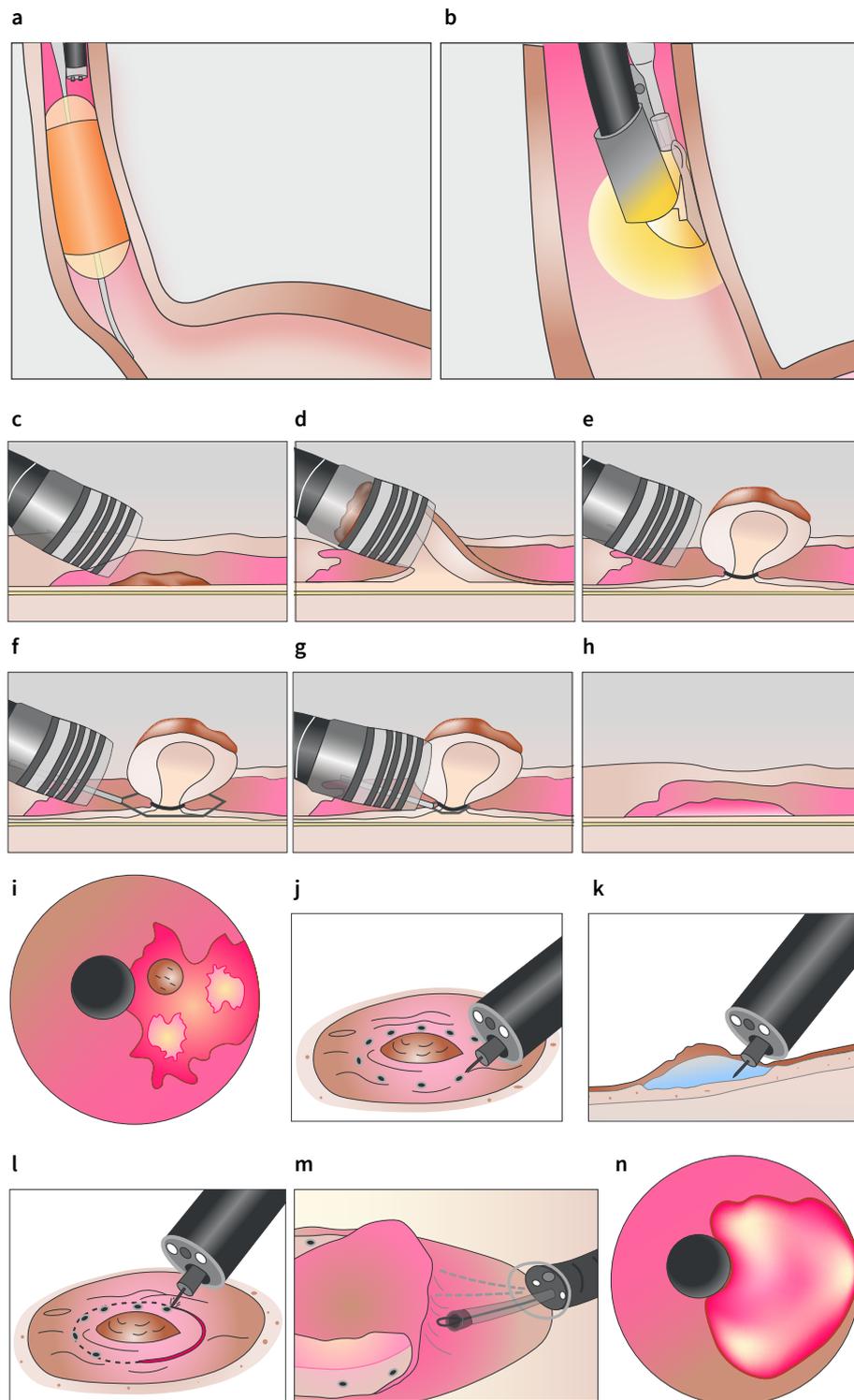


Figure 4 | Treatment of Barrett oesophagus neoplasia. **a** and **b** | Circumferential (**a**) and focal (**b**) radiofrequency ablation (RFA) is only suitable for the treatment of lesions that are not visible. **c–h** | Multiband mucosectomy (MBM) for endoscopic mucosal resection (EMR). **i–n** | Endoscopic submucosal dissection (ESD).

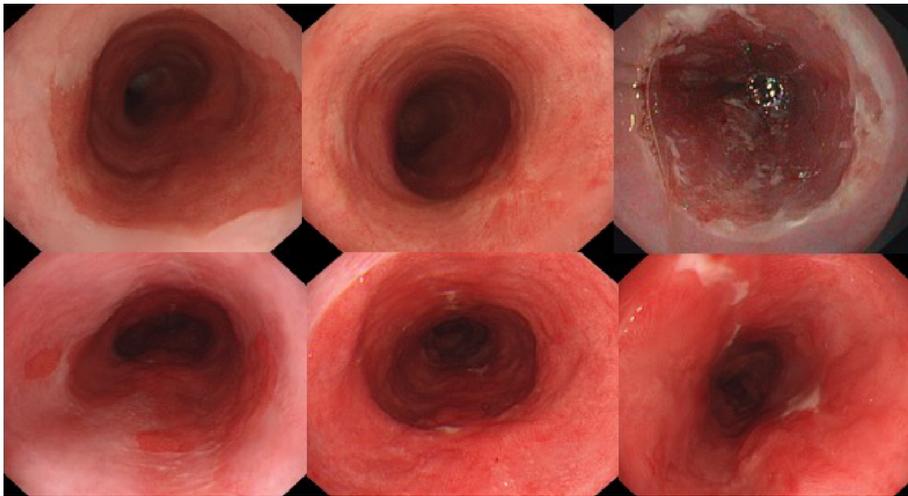


Figure 5 | A swollen oedematous Barrett oesophagus segment with exudates. After every ablation session, sufficient time should be allowed for the mucosa to heal, so that it is flat, with no exudates or swelling (as per the images in the top row). If the mucosa is not completely healed, it will be too thick for ablation to be effective and visible lesions will be missed. Endoscopic images courtesy of BEST Academia [www.best-academia.eu]

Remember that you have already resected the mucosa and a significant part of the submucosa and that applying too much pressure may lead to a perforation. A careful snare tip coagulation generally suffices, but if the bleeding continues despite two or three applications you need to switch gears to coagulation forceps. This switching will require you to release the remaining rubber bands in the stomach to allow passage of the forceps.

Most bleeds can be adequately managed with just snare-tip coagulation. After the bleeding is under control, remember to clean the surface area and to evacuate all fluids and blood from the stomach before you embark on your next resection.

Mistake 10 Making things worse in case of a post-resection perforation

Perforations after MBM in patients with Barrett's oesophagus are, thankfully, rare, occurring in 0.8–0.9% of cases (figure 6). They are never life threatening unless you make them.

If a post-resection perforation occurs while you are insufflating the oesophagus and the mediastinum, avoid spending too much time 'thinking' without actually 'doing'. Such delayed action can cause pneumothorax and pneumediastinum, and that indeed can be life threatening. If you are not already using CO₂ insufflation, then immediately switch to it. If you do not have CO₂ insufflation available, then you should not be performing therapeutic endoscopies.

In these circumstances, there are several steps that should be followed (figure 7). First, you should remove the endoscope with the resection specimen. Second, question how certain you are that you will cure the patient with your treatment. If you think you may have resected

a deep submucosal cancer, it may be best to transfer the specimen to the pathology laboratory for immediate evaluation. Taking this action can make you switch gears to the surgery that's inevitably required to manage both the neoplastic condition and the perforation, instead of managing the acute complication first and having to send the patient to surgery anyway. In the acute setting, your surgical colleague has the best chance of performing an optimal oesophagectomy. If you have to knock on their door after a week because your pathology specimen has come back with an irradically (incompletely) resected submucosal cancer while the patient is still in the intensive care unit for treatment of the mediastinitis you will rightfully be criticized for having compromised the chances of effective surgical treatment of both problems.

Third, decide whether you and your nursing

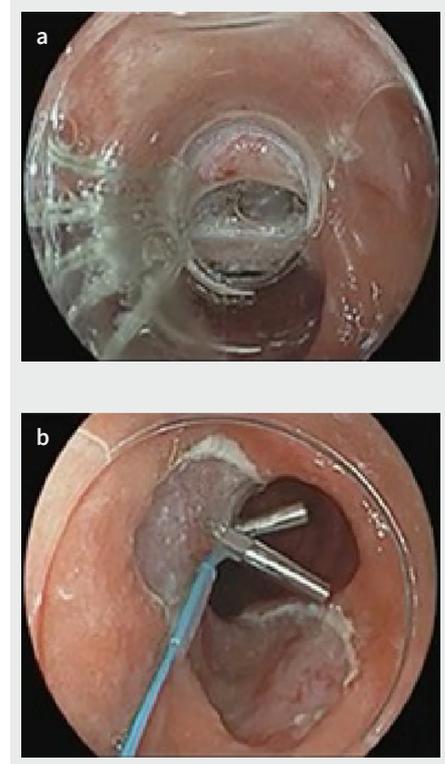


Figure 6 | Post-resection perforation. **a** | A perforation is visible inside the endoscopic resection area. **b** | The perforated area after closure with an endoloop and clips. Endoscopic images courtesy of BEST Academia [www.best-academia.eu].

team are equipped to manage the perforation if you go in again. It may be wise to optimize the endoscopic support available and/or to hand the endoscope to a more experienced endoscopist. For significant complications, we always insist on having an additional pair of endoscopist's eyes in the room to reveal any blind spots we may have. Revealing blind spots is not necessarily related to experience, so even if you are the most

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| If you are insufflating the oesophagus and the mediastinum, switch to CO ₂ insufflation | |
| 1 | Remove the endoscope with the resection specimen |
| 2 | Are you certain that you will cure the patient with your treatment? <ul style="list-style-type: none"> • It may be best to transfer the specimen to the pathology laboratory for immediate evaluation |
| 3 | Are you and your team are equipped to manage the perforation if you go in again? <ul style="list-style-type: none"> • Optimize the endoscopic support available • Consider handing the endoscope to a more experienced endoscopist • Ask for a second opinion on whether your planned approach makes sense |
| 4 | Have circumstances been optimized for the patient? <ul style="list-style-type: none"> • Intubation can avoid the most serious complications occurring • Start intravenous antibiotics |
| 5 | Know what stage of the procedure you were at when the perforation occurred |
| 6 | Consider transferring the patient to a unit with more experience with oesophageal perforations <ul style="list-style-type: none"> • Before the transfer, place a suction tube above the defect to keep the oesophagus dry • Delaying management for 24 hours will not compromise outcomes |

Figure 7 | How to approach a post-resection perforation.

experienced endoscopist in your unit we suggest you should always be prepared to ask somebody else in the room to check if your planned approach to tackle the problem makes sense.

Fourth, check whether you have optimized circumstances for the patient. In most cases it may be wise to intubate the patient to avoid the most serious complications occurring (i.e. pneumothorax and pneumomediastinum). Start intravenous antibiotics.

Fifth, know what stage of the procedure you were at when the perforation occurred. Had you finished your endoscopic resection or were you halfway through your piecemeal resection? We

generally complete the endoscopic resection before attempting to close the defect with clips or loops. In selected cases, we will bridge the defect with a stent (in case of a pre-existing stenosis, which will keep the stent in place) or with a vacuum sponge.

Finally, consider transferring the patient to a unit that has more experience in the endoscopic management of oesophageal perforations. If this is the best option, place a suction tube above the defect to keep the oesophagus dry and then transfer the patient. Be confident that delaying management for 24 hours will not compromise outcomes, whereas trying to do

something out of your league could make things significantly worse.

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Your Barrett oesophagus neoplasia briefing

UEG Week

- 'Barrett neoplasia: EMR or ESD?' presentation in the 'Therapy update: Upper GI interventional endoscopy' session at UEG Week Virtual 2021 [<https://ueg.eu/library/barrett-neoplasia-emr-or-esd/248203>].
- 'Barrett's Oesophagus: What's hot?' session at UEG Week Virtual 2021 [<https://ueg.eu/library/session/barretts-oesophagus-whats-hot/194/3034>].
- 'Endoscopic diagnosis of oesophageal neoplasia' session at UEG Week Virtual 2021 [<https://ueg.eu/library/session/endoscopic-diagnosis-of-oesophageal-neoplasia/194/2935>].
- 'Barrett's oesophagus' session at UEG Week Virtual 2020 [<https://ueg.eu/library/session/barretts-oesophagus/161/2732>].
- 'Barrett's oesophagus' presentation in the 'Screening – surveillance: Premalignant conditions' session at UEG Week Virtual 2020 [<https://ueg.eu/library/barretts-oesophagus/234493>].

- 'Mistakes in the endoscopic diagnosis and management of Barrett's oesophagus' presentation in the 'Mistakes in...' session at UEG Week Virtual 2020 [<https://ueg.eu/library/mistakes-in-the-endoscopic-diagnosis-and-management-of-barrett-s-oesophagus/234711>].
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