

Title

Treatment: Endoscopic excision of Significant Polyp and Early Colorectal Cancer (SPECC) lesions

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Abstract

Significant Polyps and Early Colorectal Cancer (SPECC) lesions are of high value to both clinicians and patients. Many of these lesions are potentially endoscopically resectable, but decision making needs to be optimised to ensure best outcomes for patients. In this review we consider: en bloc versus piecemeal resection; Endoscopic Mucosal Resection (EMR) versus Endoscopic Submucosal Dissection (ESD) including small incision EMR and hybrid ESD; adjuncts to improve resection including special snares (spiral and flat band) and new lifting solutions; and post-resection considerations including tattooing and post-polypectomy site checks. We also emphasise the importance of lesion assessment in guiding these decisions, and the need to consider other members of the SPECC multidisciplinary team, including surgeons and pathologists, in making optimal decisions for patients for these challenging lesions.

What does this paper add to the literature?

This review gives specific detailed guidance on how to approach and make choices how to endoscopically resect significant polyps and early colorectal cancer (SPECC) lesions, and how to consider the management of these lesions as part of a wider SPECC multidisciplinary team.

Main Manuscript

Endoscopic assessment

Experience and diagnostic competence in lesion assessment is the cornerstone of correct decision making for endoscopic excision, with key features to be familiar with including: size, lesion morphology, surface features, and lesion complexity, described above (see Rutter Size shape access etc.)([1]. En bloc excision is preferred but needs to be balanced against risks and patient wishes, with piecemeal Endoscopic Mucosal Resection (EMR) remaining the key technique for most low risk colorectal lesions. Hybrid EMR-ESD (Endoscopic Submucosal Dissection) techniques can offer advantages of each and are likely to see wider use.

Pedunculated lesions

Pedunculated lesions should usually be removed en bloc by transection through the stalk composed of normal mucosa. Lesions that contain early invasive components i.e. Haggitt classification level 1-3 without lymphovascular invasion are usually considered curative excisions by endoscopic resection[2]. It is therefore critical to resect such lesions relatively low on the stalk to ensure that the pathologist can assess the stalk and report a clear margin to the invasive component; however this needs to be balanced against the increased risk of a full thickness diathermy injury when resection is closer to the bowel wall. To avoid the latter, the stalk may be resected with less diathermy energy thus increasing the risk of bleeding, necessitating stalk pre-injection with adrenaline, and the use of mechanical haemostasis with clips or loops[3]

Sessile and flat lesions

En bloc versus piecemeal resection

En- bloc resection is generally to be preferred as it provides a higher quality pathological specimen that allows a more precise pathological determination of whether there may be an early invasive component to the lesion, and lower recurrence rates; however, en- bloc resection techniques are associated with higher risks, especially of perforation, and increased procedural difficulty and time (for ESD), which needs to be balanced against the potential benefits. Piecemeal techniques are faster, safer and need less procedural skill, and are therefore appropriate for lower risk lesions e.g. Granular type laterally spreading tumours (LST) without high risk features. Lesions with higher risk features e.g. Granular type LST with a large nodule may still be resected piecemeal, but the area with the large nodule should be carefully resected as a large piece en- bloc and submitted separately to the pathologist.

Endoscopic mucosal resection (EMR)

This technique involves injecting a solution, traditionally saline, under the lesion to expand the submucosal space and elevate the lesion away from the muscle layer below. This can

also make flat lesions more bulbous and easier to grip. Changes to the solutions injected have made the lifting longer lasting and helped clarify lesion edges (see adjuncts below)

The presence or absence of lifting is a further important feature that can alter decision making at the point of endoscopic resection. Submucosal lifting of lesions can give an indication of invasive risk. Tumour invasion into the submucosal and associated desmoplasia and fibrosis can tether a lesion leading to the “non-lifting sign”, where all or part of a lesion is not elevated by submucosal injection[4]. Multiple biopsies, prolapse, previous attempts at resection or scarring e.g. in a patient with colitis can mimic this process and therefore judgement is called for in the interpretation of lifting; however in a lesion that has not been previously manipulated, especially if in concert with high risk features described above¹ [Rutter], deep submucosal invasion should be suspected, which is usually an indication to abandon endoscopic excision.

EMR for lesions 20mm or less in size in the colon, and up to 25mm in the rectum, should usually aim for a resection specimen en bloc[5]. Effective injection to lift the lesion is critical here, especially the use of a “dynamic” injection technique to maximise lift under the lesion. This involves active manipulation of the injection catheter during the injection process, usually lifting the tip up into the lumen as the lift develops, with suction to reduce mucosal tension, avoiding lateral dispersal of the lifting solution[6]. Gripping a large lesion for en bloc EMR can be challenging and special snares that aid grip may help (see adjuncts). A specific technique that can be helpful in this situation is the use of the “small incision” (SI) technique[7]. Here, post lifting, the tip of the snare is used to make a small lateral incision a few millimetres in size on the oral side of the lesion. The tip of the snare is placed into the incision to anchor it while the snare is slowly opened around the lesion, ensuring that the snare does not slip at the back of the lesion when out of view during snare closure, improving the chance of en bloc resection.

For lesions larger than 20mm, piecemeal EMR (pEMR) simply joins up multiple resections across the polyp to remove the whole lesion comprehensively. It is rapid, effective and safe and is used for the majority of low risk colorectal lesions. Injecting and lifting the lesion in stages is preferred to a single lift of the whole lesion that is not maintained. Fewer larger pieces are preferred to minimise recurrence risk, and a small amount of normal mucosa is usually taken at the edge of the lesion to try and reduce recurrence risk. A recent study that looked at taking an extra large rim of normal mucosa did not reduce recurrence; however the use of ablation at the lesion edge, either with argon plasm coagulation or soft coagulation, does appear to reduce recurrence risk.

Traditional teaching has recommended starting with the section of the lesion that is hardest to access, often on the oral side of the lesion; however so long as the endoscopist is confident all the lesion can be accessed, removing tissue starting at the anal side can help start a clear resection plane and allow the use of the previous resection edge (divot) as an anchor point for the snare and allow accurate snare placement to avoid mucosal “islands”.

Lesions 40mm or more in size, or that are otherwise complex, (see SMSA classification Rutter above) are recommended for referral to specialist centres, usually via a complex polyp / SPECC MDT[5].

Endoscopic submucosal dissection (ESD)

ESD as a relatively new technique for Western endoscopists that offers en bloc mucosal excision. This has the benefit of a high quality pathological specimen which allows accurate determination of deep and lateral margins of a lesion and the depth of submucosal invasion, if present. Lesions with invasion which is <1000um, and without lymphovascular invasion and poor differentiation, are considered to be at such low risk of lymph node metastasis that bowel resection is not recommended, and such resections are curative[8] Recurrence rates are essentially zero when a pathologically confirmed en bloc R0 resection is achieved; however this needs to be balanced against significantly increased procedural difficulty, a higher risk of perforation (although usually managed non-surgically with endoscopic clips), and a much greater procedure time. Typically EMR takes 20-30 minutes compared to 1-2 hours for ESD. Therefore ESD is usually reserved for higher risk lesions e.g. those with a large nodule or depressed component, Kudo type Vi pit pattern without a demarcation line, or very large lesions >40mm, especially in the rectum, where recurrence rates post EMR are high. Lower volume centres (<10 ESD cases per year) had lower rates of en bloc resection and were more likely to have prolonged procedure times beyond 2 hours [9]; however, there was no differences in EMR outcomes at lower volume centres (<50 cases per year) compared with higher volume centres [10].

Classical ESD involves lifting the lesion, mucosal incision, making a “groove” down to the muscle layer, submucosal dissection, elevation of a mucosal flap, and completing the resection en bloc; however many of the benefits of classical ESD can be obtained more quickly and with less technical skill by using “hybrid” ESD also described as “simplified” or “universal” ESD. In this technique, the mucosal incision and groove part of classical ESD are performed as usual, and some submucosal dissection may be performed. However once the lesion had a clear “grippable” edge, and is smaller than 25mm, after maximal lifting, a snare is placed within the mucosal groove and closed to complete the resection en bloc[11].

Adjuncts to resection

Lifting is a key part of EMR and ESD, and effective lifting by injection under the lesions can greatly facilitate the resection. Although saline was used classically, other solutions have been tried which can enhance this process. Colloids e.g. Gelofusine are widely available and persist in the mucosa for longer than plain saline and have been widely adopted. Other injectates e.g. sodium hyaluronate (Sigmavisc, Diagmed Ltd. United Kingdom)) which are more viscous but provide a much longer and sustained lift are available but are more expensive, traditionally used in ESD, but also now for complex EMR[12]. Very recently new injectates which have differing viscosities at different temperatures are available that at room temperature have water like viscosity, but form a gel at body temperature providing very long lasting lift e.g. Eleview (Aries Pharmaceuticals, USA)[13].

Many endoscopists also include low concentration adrenaline in the lifting solution e.g. 1:1in 200,000 adrenaline to avoid minor mucosal ooze and keep the resection field clear. It is also commonplace to have low concentration methylene blue or indigocarmine in the injection solution which provides negative contrast to enhance visibility of lesion edges.

Some snares can provide enhanced grip for flat or fibrotic lesions to support EMR. Braided snares have an additional wire around the main snare cable giving enhanced friction to aid gripping (Spiral snare, SnareMaster, Olympus, Japan). “Flat band” or ribbon monofilament snares are a vertical ribbon of metal, whose sharp edge provides very high levels of grip, though less haemostasis (ResectionMaster, Medwork, Germany). Care needs to be taken with such snares that the enhanced grip does not lead to gripping muscle below the lesion thus leading to perforation.

Post resection

By definition SPECC lesions have a risk of cancer and therefore endoscopists need to mark lesions that may require surgical resection. After effective endoscopic resection this may mean there is no residual lesion for the surgeon to feel, and as much of this subsequent surgery is likely to be laparoscopic, clear marking is critical. We recommend at least two tattoos, 2-3cm (one fold) on the anal side of the resection site on opposite walls of the bowel with sterile carbon particles e.g. SPOT[®]. Care should be taken to achieve submucosal injection e.g. by injecting into a bleb of saline to avoid contaminating the peritoneal cavity with carbon particles. Injection of a dye too close to the lesion, either before endoscopic resection or afterwards, can lead to severe submucosal fibrosis which can substantially hinder endoscopic resection. Caecal lesions are anatomically identifiable enough not to need tattooing, and we suggest avoiding tattooing within 20cm of the anal verge as carbon particles within the mesorectum can make surgical resection more difficult.

After endoscopic resection we recommend endoscopic follow up at 3-6 months, at 12-18 months and then at 3 years from the original resection date. Recurrence rates at 6 months of approximately 20% are reported after piecemeal EMR, with further recurrence appearing at later dates even if the 6 month site check was clear [14].

Conclusion

Even very large SPECC lesions can be resected endoscopically with high success rates and low morbidity, and almost no mortality. Choice of technique should be personalised to the patient as well as individualized to the lesion. Endoscopists should consider the challenges faced by pathologists (and therefore aim for en bloc resection) and by surgeons (with optimal documented endoscopic marking) as part of the wider SPECC team when assessing and managing SPECC lesions.

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