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Endoscopic Mucosal Resection (EMR) Versus Endoscopic Submucosal Dissection (ESD) for Resection of Large Distal Non-Pedunculated Colorectal Adenomas

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Abstract---Background: Endoscopic mucosal resection (EMR) is currently the most used technique for resection of large distal colorectal polyps. However, in large lesions EMR can often only be performed in a piecemeal fashion resulting in relatively low radical (R0)-resection rates and high recurrence rates. Endoscopic submucosal dissection (ESD) is a newer procedure that is more difficult resulting in a longer procedural time, but is promising due to the high en-bloc resection rates and the very low recurrence rates. Objective: To investigate whether Endoscopic mucosal resection (EMR) is superior to endoscopic submucosal dissection (ESD) for resection of large distal non-pedunculated colorectal adenomas. Methods: PubMed, Google scholar and Science direct were searched using the following keywords: Endoscopic mucosal resection, endoscopic submucosal dissection and Colorectal adenomas. The authors also screened references from the relevant literature, including all the identified studies and reviews, only the most recent or complete study was included. Documents in a language apart from English have been excluded as sources for interpretation was not found. Papers apart from main scientific studies had been excluded: documents unavailable as total written text, conversation, conference abstract papers and dissertations. Conclusion: EMR is safe and effective for treating colorectal adenomas.

Keywords---colorectal adenomas, colorectal polyps, endoscopic mucosal resection, endoscopic submucosal dissection.

Introduction

Resection of colorectal adenomas has shown to lower the mortality rate due to colorectal cancer with 60 % [1]. Especially large adenomas maintain a high risk of progression to invasive cancer, underlining the importance of adequate resection [2]. Endoscopic resection of large adenomas has been proven to be feasible and safe, with less morbidity, mortality and costs compared to surgical resection [3]. Endoscopic resection of non-pedunculated adenomas is most often performed using the 'lift-and-cut' endoscopic mucosal resection (EMR) technique [4]. However, in adenomas larger than 2 cm in size EMR can often only be performed in a piecemeal fashion (pEMR) due to the limited size of the snare, difficulty to position the endoscope, and often extension of the polyp over one or multiple folds [5]. Although safe, piecemeal resection lowers the reliability of assessing the dysplasia free resection margins (R0 resection) at histology. This is also reflected by the relative high recurrence rate at follow-up colonoscopy after EMR ranging between 12-16 %, and even increasing up to 30 % in non-pedunculated polyps exceeding 40 mm in size [6, 7].

Endoscopic mucosal resection (EMR) is widely used in Western centers for the treatment of non-pedunculated colorectal adenomas >2 cm in size. Colonic endoscopic submucosal dissection (ESD) for the treatment of these adenomas is rarely performed outside of Japan and Korea [8]. EMR is associated with a low risk of adverse events, rapid procedure times, and relatively low technical complexity; it is also suitable for outpatient treatment as patients generally only need to be observed for a few hours after the procedure and can go home the same day [7]. ESD is technically complex, involves a long procedure time, and is associated with a significant risk of intraprocedure and delayed colon perforation; patients require hospitalization for observation after the procedure [9]. The main advantage of ESD is the excellent rate of en bloc resection, which reduces local recurrence rates and ensures precise histopathologic staging if malignancy is detected. However, advances in endoscopic optics have improved the visual assessment of malignancy, and improvements in endoscopic techniques have significantly reduced the local recurrence rate after EMR and facilitated the treatment of recurrences. EMR is therefore likely to continue as the widely used technique for the treatment of large colorectal adenomas [10].

Definition EMR and ESD

EMR is performed with a snare to capture the target tissue. An electrosurgical current is then used to transect the tissue that has been grasped, although recently a cold snare EMR has been described. Injection is usually given in the submucosal space to elevate the lesion but is not always necessary; some techniques, such as underwater EMR, do not require injection into the submucosa. If the lesion is larger than 15 to 20 mm, it typically has to be removed in piecemeal fashion. The main use of EMR is to remove dysplastic polyps that are larger than 10 mm [11].

ESD is performed by injecting fluid into the submucosa and creating an incision around the perimeter of the lesion, and then carefully dissecting the lesion from the deeper layers. Various specialized instruments (ESD knives) are utilized to

perform the procedure. The use of ESD continues to evolve as the technique improves. In Japan and Europe, there are guidelines that provide specific recommendations on the appropriate use of ESD. Although there are subtle differences between the 2 guidelines, generally speaking, ESD is endorsed for lesions that have a high likelihood of cancer invading the superficial submucosa and for lesions that cannot be removed by EMR due to fibrosis in the submucosal space or post-EMR recurrences. At present, there are no US-specific guidelines for the use of ESD [11, 12].

Investigation

Endoscopic mucosal resection (EMR) is the current standard for the treatment of large colorectal polyps and has been shown to reduce colorectal cancer-related mortality [13]. The European Society of Gastroenterology (ESGE) recommends EMR with submucosal injection for the resection of sessile or flat polyps of ≥ 10 mm in size [14]. However, one limitation of EMR is its association with low en bloc resection rates, especially for polyps larger than 10 mm. Piecemeal resection is one of the main reasons for adenoma recurrence, with local recurrence rates of 15% to 30% on follow-up colonoscopy [15, 16].

Endoscopic submucosal dissection (ESD), as an alternative approach, allows the en bloc resection of large polyps and has shown significantly lower recurrence rates compared to EMR [17]. According to the ESGE guidelines, ESD should be considered for complex lesions with a high suspicion of submucosal invasion, such as 0-IIc or 0-IIa/0-IIc lesions, as well as nongranular-type lesions, larger than 2 cm, that may harbor superficial multifocal submucosal invasion [18]. However, ESD is not widely practiced in Western countries, because it is time-consuming, requires advanced skills and prolonged training, and is associated with higher complication rates compared to endoscopic mucosal resection (EMR), especially in the colon [19, 20].

For this reason endoscopic submucosal dissection (ESD) was developed in Japan, a technique that enables to achieve en-bloc resection even in large polyps [21]. Several retrospective observational studies compared EMR and ESD. A recent meta-analysis pooled the results yielding a total of 2299 lesions [22]. Although studies were biased by baseline differences with special regard to tumor location and polyp size due to lack of a randomized design, results are promising. Rates of en bloc resection and radical resection were much higher, and the rate of recurrence was much lower in the ESD-group (91.7, 80.3 and 0.9 % respectively) than in the EMR-group (46.7, 42.3 and 12.2 % respectively). This benefit comes at the expense of an about three-fold longer procedure time and more complications (perforation rate 5.7 % versus 1.4 %). However, this safety profile may be favorable in the distal colon, given the lower risk for complications as compared to proximally located polyps [23].

Advantages and disadvantages associated with each technique

Each technique has its own advantages and disadvantages. EMR is relatively simple to perform, uses a limited number of devices, and has a long track record of being successful for the majority of dysplastic, precancerous lesions. The main

disadvantage of EMR is that piecemeal resection is required for larger lesions, which precludes, in some cases, accurate histopathologic evaluation and may compromise a cure. As a result, some patients who are treated with EMR may require additional surgery, whereas if they had been treated with ESD, they may have been cured. The other major disadvantage of EMR is that it has a high lesion recurrence rate in the range of 15% to 20%, which necessitates further therapy [11, 12].

The main advantage of ESD is that it allows en bloc resection of any type of lesion regardless of size. Removing the entire lesion in a single piece is a basic oncologic principle and carries the benefits of accurate histologic assessment and staging, determination of curative resection, and a very low recurrence rate of less than 1%. However, ESD is technically more demanding than EMR and requires advanced endoscopy skills. Furthermore, ESD is a longer procedure associated with a higher perforation rate compared to EMR. Fortunately, the vast majority of perforations caused by ESD can be successfully treated by endoscopy without the need for surgery [11, 12].

New advances in EMR

Increased experience and improved endoscopic imaging using higher resolution cameras, dual focus design allowing closer inspection, and proprietary imaging techniques (narrow band imaging, blue laser imaging, and iScan) show significant promise in improving the endoscopic differentiation of benign and malignant colorectal lesions. This may influence treatment planning, as piecemeal resection with EMR is generally considered acceptable for benign adenomas, but en bloc resection should be performed for malignancies [24]. Avulsion, a newly described technique utilizing hot biopsy forceps with cutting current, enables complete removal of many fibrotic islands of residual adenoma encountered during EMR. In a comparative analysis involving argon plasma coagulation, the use of avulsion resulted in significantly higher rates of complete removal of all visible neoplasia during EMR and markedly reduced recurrence rates [10].

Thermal ablation of the margin of the resection site after EMR can potentially reduce the incidence of recurrence by ablating microscopic areas of non-visible residual adenoma. Preliminary results from a multicenter randomized study presented in abstract form in 2016 demonstrated a reduction in adenoma recurrence from 20% to 6% with thermal ablation of the margin [25]. Underwater EMR is another recently described technique in which colorectal adenomas are removed using a snare underwater, without submucosal injection [26]. Underwater EMR is particularly well suited for non-lifting lesions with fibrosis from prior incomplete resection attempts or other manipulations. In this setting, it increases the complete resection rate of visible neoplasia and reduces recurrence [27]. Successful underwater en bloc snare resection of 2- to 4-cm large adenomas has also been reported, challenging the conventional approach of avoiding en bloc snare resection of lesions >2 cm due to the fear of perforation [28]. If ongoing studies confirm the excellent efficacy and safety profile of this initial report, underwater en bloc resection may become more widely adopted.

Treatment of recurrences after EMR

The majority of recurrences after EMR are unifocal and <5 mm in size. Over 90% of the recurrences can be treated with conventional snare polypectomy, EMR, or ablation [16]. A second recurrence is found in 10% to 40% of all patients after treatment of the first recurrence [16, 27]. Underwater EMR appears to be superior to conventional EMR for treating recurrences, with a higher rate of complete removal of visible neoplasia and a lower second recurrence rate [27]. Even lesions that recur two or more times can be treated successfully with additional EMR or underwater EMR [29]. Treatment of recurrences with EMR or underwater EMR appears to be as safe as the treatment of naive lesions, with a low risk of bleeding or perforation [16, 27, 29]. Progression to malignancy during treatment is very rare [16, 29].

Endoscopic mucosal resection

Multiple large observational studies have documented the safety and efficacy of EMR for the treatment of non-pedunculated colorectal adenomas >2 cm in size. The prospective multicenter Australian Colonic EMR (ACE) study demonstrated an intention-to-treat rate of 84% of successful EMRs with a mean procedure duration of 25 minutes [7]. Submucosal invasive cancer was found in 6.9% of the cases and was generally treated with surgery. The adverse event rate was 7.7%: 2.1% of the cases required overnight hospitalization for post-procedure pain, 1.5% required a 3 to 5 day hospitalization and antibiotics for serositis, 2.9% required hospitalization for post-procedure bleeding, and 1.3% developed a perforation. A subsequent publication that included more patients and more extensive follow-up demonstrated a local recurrence rate of 16% at 4-month follow-up, with an additional 4% recurrence rate found at 16 months [16]. Risk factors associated with recurrence include lesion size >40 mm; use of argon plasma to ablate residual adenoma not amenable to snare resection; and prior manipulations leading to fibrosis, such as partial snare polypectomy, tattoo application at the site of the lesion, or aggressive biopsies of the lesion [9].

Comparison of EMR and ESD

In expert centers, ESD enables complete en bloc resection of >85% of all colorectal adenomas and superficial cancers [9]. In contrast, en bloc resection rates for colorectal adenomas >2 cm in size are typically 25% or less with EMR [30]. Adenoma recurrence is significantly more common with EMR than with ESD: recurrence rates for adenomas >2 cm in size treated with EMR are typically approximately 16% in Western centers [16] and 7% in Japanese centers [29], while recurrence rates with ESD are 1.4% in Japan [29]. However, ESD requires significantly longer time to perform than EMR: the mean procedure time for EMR in a large Western study was 25 minutes while that for ESD in a large Japanese study was 116 minutes [9]. In the same two studies, perforation occurred in 1.3% of the patients undergoing EMR and in 4.9% of the patients undergoing ESD. Hospitalization was required in <10% of the Western patients who underwent EMR, while 100% of Japanese patients undergoing colorectal ESD are typically hospitalized for >3 days [31].

While piecemeal EMR of adenomas results in good clinical outcomes in most patients, en bloc resection with ESD is preferable for cancers with slight submucosal invasion and favorable histologic features, as it provides curative endoscopic treatment without the need for surgery [32]. Piecemeal resection with EMR may reduce the accuracy of histologic analysis and may lead to poor oncologic outcomes due to local recurrence. With current technology, endoscopic differentiation between adenoma and cancer is only 70% to 90% accurate, and the accuracy of differentiating between slight and deep submucosal invasion is only 70% to 80%; therefore, precise histologic staging with an en bloc resection using ESD is preferable for lesions that have a significant likelihood of being invasive cancers [32].

Conclusion

EMR is safe and effective for treating colorectal adenomas. Compared with ESD, EMR is significantly faster to perform, has a much lower perforation rate, and does not require post-procedure hospitalization. Currently, endoscopic resection techniques are the preferred modality for management of dysplastic and early cancer lesions throughout the gastrointestinal tract. Both ESD and EMR contribute to the successful management of these lesions, and each patient needs to be treated with the most appropriate technique in his or her case.

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