MINI REVIEW

Our perspective on endoscopic resection for colorectal neoplasms

T. Matsuda\textsuperscript{a, *}, T. Gotoda\textsuperscript{a,b}, Y. Saito\textsuperscript{a}, T. Nakajima\textsuperscript{a}, M. Conio\textsuperscript{c}

\textsuperscript{a} Endoscopy Division, National Cancer Center Hospital, 5-1-1 Tsukiji, Chuo-ku, Tokyo 104-0045, Japan
\textsuperscript{b} Department of Gastroenterology & Hepatology, National Center for Global Health and Medicine, Tokyo, Japan
\textsuperscript{c} Department of Gastroenterology, CHU St.-Antoine, Paris, France

Available online 23 June 2010

Summary Endoscopic mucosal resection (EMR) is a minimally invasive technique for effective treatment of early stage colorectal lesions with no invasive potential. However, the high frequency of local recurrence after piecemeal EMR for large lesions is considered a serious problem. In contrast, endoscopic submucosal dissection (ESD) allows \textit{en-bloc} resection, irrespective of the lesion’s size. ESD has been established as a standard method for the endoscopic removal of early cancers in the upper gastrointestinal tract in Japan. Although the use of ESD for colorectal lesions has been studied clinically, ESD is not yet established as a standard therapeutic method. We define the indications for \textit{en-bloc} resection, based on extensive clinicopathological analyses, as a laterally spreading tumor (LST) non-granular type (LST-NG) lesion greater than 20 mm and an LST granular (LST-G) type lesion greater than 40 mm. Both of these lesions had a high submucosal invasion rate. Especially, LST-NG type lesions greater than 20 mm are technically difficult to remove completely even by piecemeal EMR and are considered a “definite indication for \textit{en-bloc} resection”\textsuperscript{1}. The ESD procedure is undoubtedly an ideal method to achieve \textit{en-bloc} resection, however, the prevalences of suitable lesions among all neoplastic lesions and among all early cancers were not high (1.0\% and 5.0\%, respectively). Therefore, it is crucial to master more fundamental therapeutic techniques and have knowledge of surveillance strategy after endoscopic treatment.

© 2010 Elsevier Masson SAS. All rights reserved.

Introduction

Colorectal cancer is the third most important cause of cancer mortality in Japan\textsuperscript{1}. The recognition and removal of early stage colorectal cancer and precancerous lesions are considered to be important for control of colorectal cancer\textsuperscript{2}. Endoscopic mucosal resection (EMR) is now a well-established technique worldwide for the treatment of colorectal neoplasms with minimal invasiveness\textsuperscript{3–6},...
however, the high frequency of local recurrence after piecemeal EMR for large lesions is considered a serious problem [7,8]. To avoid this problem, Japanese endoscopists developed a new technique that allows en-bloc resection of larger colorectal lesions. This technique, known as endoscopic submucosal dissection (ESD), starts with the submucosal injection, followed by dissection beginning at the lateral edges and working through the submucosal layer until the lesion is removed in one piece. Despite its longer procedure time and higher complication rate, ESD resulted in a higher en-bloc resection rate compared to that seen with conventional or piecemeal EMR [9–11]. This paper summarizes recent data of colorectal neoplasms, indications for en-bloc resection, and prevalence of candidate lesions among all early stage colorectal neoplasms from the database of National Cancer Center Hospital, Tokyo, Japan.

**Indication criteria for endoscopic treatment**

EMR is indicated to treat intramuscular colorectal cancer because the risk of lymph node metastasis is nil [12,13]. Surgery is indicated to treat submucosal invasive cancers because of the 6–12% risk of lymph node metastasis [14–18]. There is increasing evidence, however, to suggest that lesions with submucosal invasion less than 1000 μm — without lymphovascular invasion and without poor differentiation — also have a minimal risk of lymph node metastasis [19] and can be cured by EMR alone. Though lymphovascular invasion and poorly differentiated adenocarcinoma components are impossible to predict before resection, the vertical depth of invasion of submucosal cancers can be estimated based on the morphologic appearance at the time of endoscopy. It is therefore quite important to be able to distinguish neoplasms that are candidates for EMR from those that will require surgery, because EMR of lesions containing massive submucosal invasive cancer is associated with the risks of bleeding and perforation and is unlikely to be curative.

**Current status of colorectal EMR and limitations**

EMR is a minimally invasive technique for effective treatment of early stage colorectal lesions with no invasive potential. Several EMR techniques have been described (i.e. strip biopsy [inject, lift, and cut method], cap-assisted EMR [EMR-C], EMR with ligation [EMR-L]). The “inject and cut” method is simple and safe and is used widely for colorectal neoplasms. Lesions that do not lift during submucosal injection are generally not candidates for resections using the standard EMR technique. Due to the size of the snare, cap, and ligation device, these EMR techniques cannot be used to remove larger than 2 cm in one piece. This limitation prevents precise histopathological assessment and increases the risk of local recurrence. For such large colorectal lesions endoscopically diagnosed as intramuscular or submucosal superficial (<1000 μm) invasion, piecemeal removal is possible, however, studies have shown that the risk of local recurrence is 2.7–23.5% [9–11]. Varying frequencies have been reported across institutions, probably related to the resection technique and varying abilities to judge for a diminutive residual tumor after piecemeal EMR. However, it has been proved that almost all local residual recurrences are not serious problems, because they are adenomatous lesions that have developed from the edge of primary lesions and can be managed by additional endoscopic treatment if vigilant follow-up is carried out [9,10,20]. The length of a suitable interval of surveillance colonoscopy after piecemeal EMR is still controversial (2–6 months) [21].

**Endoscopic depth diagnosis and definite indication for “en-bloc” resection**

Estimation of the depth of cancer invasion before treatment is crucial to decide the therapeutic plan. New diagnostic modalities such as endoscopic ultrasonography using mini-probe and magnifying chromoendoscopy are reported to be useful for the depth diagnosis of early colorectal cancers. However, these modalities are relatively expensive and time consuming. Therefore, if invasion depth could be diagnosed with only conventional colonoscopy, it would be more cost effective and convenient. Saitoh et al. reported that characteristic colonoscopic findings obtained by a combination of videocolonoscopy and chromoendoscopy are clinically useful for determination of the invasion depth of depressed type colorectal cancers [22]. In this report, characteristic colonoscopic findings (i.e. [1] expansion appearance, [2] deep depression surface, [3] irregular bottom of depression surface, and [4] folds converging toward the tumor) suggested the need for surgical treatment.

Magnifying chromoendoscopy is a standardized, validated method that facilitates detailed analysis of the morphological architecture of colonic mucosal crypt orifices (pit pattern) in a simple and efficient manner. The clinical classification of the colonic pit pattern (invasive and noninvasive) by using magnifying chromoendoscopy was originally described by Fuji et al. with the aim to discriminate between intramuscosal-submucosal superficial invasion and submucosal deep invasion [23]. The existence of a non-invasive pattern as determined by magnifying chromoendoscopy is the minimum requirement for all lesions that are candidates for endoscopic treatment [24]. An invasive pattern is characterized by irregular and distorted pits observed in a demarcated area suggesting submucosal deep invasion (> 1000 μm).

We define the indications for en-bloc resection, based on extensive clinicopathological analyses [25], as a laterally spreading tumor (LST) non-granular type (LST-NG) lesion greater than 20 mm and an LST granular (LST-G) type lesion greater than 40 mm. Both of these lesions had a high submucosal invasion rate (Table 1). Especially, the LST-NG type lesion greater than 20 mm is technically difficult to remove completely even by piecemeal EMR; we define these lesions as a “definite indication for en-bloc resection”. In contrast, LST-G type lesions greater than 40 mm are considered a “relative indication for en-bloc resection”. Moreover, large villous tumors, recurrent lesions, and residual intramuscular lesions showing non-
**Table 1** Relationship between size of LSTs and rate of submucosal invasion National Cancer Center Hospital, Tokyo, 1998–2006.

<table>
<thead>
<tr>
<th>Size (mm)</th>
<th>IIa (LST-G)</th>
<th>Is + IIa (LST-G)</th>
<th>Ila (LST-NG)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>0/115 (0)</td>
<td>4/72 (5.6)</td>
<td>12/246 (4.9)</td>
</tr>
<tr>
<td>20</td>
<td>0/70 (0)</td>
<td>6/70 (8.6)</td>
<td>24/106 (22.6)</td>
</tr>
<tr>
<td>30</td>
<td>1/31 (3.2)</td>
<td>9/65 (13.8)</td>
<td>11/33 (33.3)</td>
</tr>
<tr>
<td>40</td>
<td>0/13 (0)</td>
<td>25/114 (21.9)</td>
<td>8/17 (47.0)</td>
</tr>
<tr>
<td>Total</td>
<td>1/229 (0.4)</td>
<td>44/321 (13.7)</td>
<td>55/402 (13.7)</td>
</tr>
</tbody>
</table>

LST-G: laterally spreading tumor, granular type; LST-NG: laterally spreading tumor, non-granular type.

**Table 2** Prevalence of LSTs and indicated lesions for ESD National Cancer Center Hospital, Tokyo, 2000–2006.

<table>
<thead>
<tr>
<th>Lesion</th>
<th>All neoplastic lesions % (n=11,488)</th>
<th>Early colorectal cancers % (n=1691)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LSTs²</td>
<td>5.9 (674)</td>
<td>22.6 (382)</td>
</tr>
<tr>
<td>Indication for ESD²</td>
<td>2.3 (267)</td>
<td>12.1 (205)</td>
</tr>
<tr>
<td>Definite indication for ESD³</td>
<td>1.0 (115)</td>
<td>5.0 (85)</td>
</tr>
<tr>
<td>Relative indication for ESD³</td>
<td>1.3 (152)</td>
<td>7.1 (120)</td>
</tr>
</tbody>
</table>

² LSTs: LST-G and LST-NG.
³ Definite indication: LST-NG lesion ≥ 20 mm.

Lifting sign after EMR were also potential candidates for ESD.

**ESD procedures**

The ESD procedure is undoubtedly one of the ideal methods to achieve *en-bloc* resection. In our center, ESD procedures are primarily performed using a bipolar knife (B-knife) [26] or an IT knife with carbon dioxide (CO₂) insufflations instead of air insufflations to reduce patient discomfort [10,27,28]. Lesion margins are delineated before ESD by using 0.4% indigo-carmine dye spraying. After injection of Glyceol® (10% glycerol and 5% fructose in normal saline solution) [29] and sodium hyaluronate acid into the submucosal layer [30], a circumferential incision is made using the B-knife and ESD is then carried out using both the B-knife and IT-knife.

**Prevalence of "definite indication" for ESD-data from National Cancer Center Hospital, Tokyo**

Between January 2000 and December 2006, a total of 11,488 colorectal neoplasms (except advanced cancers) in 6369 patients were treated endoscopically or surgically at the National Cancer Center Hospital, Tokyo. To clarify the prevalence of "definite indication for colorectal ESD", we reviewed and analyzed records from our database. There were 9797 adenomas and 1691 early colorectal cancers (intramucosal cancer: 1294, submucosal cancer: 397). Among all neoplastic lesions, the prevalence of LSTs (LST-G and LST-NG) and the proportion for which ESD would have been indicated were 5.9% and 2.3%, respectively (Table 2). In contrast, among all early cancers, the prevalence of LSTs was 22.6% and proportion for which ESD would have been indicated was 12.1%. Moreover, the prevalences of "definite indication for ESD" among all neoplastic lesions and all early cancers were 1.0% (115/11,488) and 5.0% (85/1691), respectively.

**Conclusion**

The ESD procedure is an ideal method to provide "en-bloc resection" even for large colorectal lesions, however, the prevalence of lesions with a "definite indication for ESD" among all colorectal neoplasms is limited. In addition, although the use of ESD for colorectal lesions has been studied clinically, ESD is not yet established as a standard therapeutic method. Therefore, it is crucial to master more fundamental techniques (e.g. hot biopsy, snare polypectomy, conventional EMR, piecemeal EMR) and have knowledge of surveillance strategy after endoscopic treatment.

Furthermore, characteristic colonoscopic findings obtained by a combination of conventional colonoscopy and magnifying chromoendoscopy are useful and clinically important for determination of the invasion depth of early stage colorectal cancers, an essential factor in selecting a treatment modality (i.e. endoscopic treatment or surgical operation). As the therapeutic techniques are developed, preoperative endoscopic diagnosis will become more and more important.

**Conflict of interest**

The authors have not declared any conflict of interest.

**References**


