<table>
<thead>
<tr>
<th><strong>Title</strong></th>
<th>Endoscopic submucosal dissection vs laparoscopic colorectal resection for early colorectal epithelial neoplasia</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Author(s)</strong></td>
<td>Hon, SS; Ng, SS; Wong, CLT; Chiu, PW; Mak, TW; Leung, WW; Lee, JF</td>
</tr>
<tr>
<td><strong>Citation</strong></td>
<td>World Journal of Gastrointestinal Endoscopy, 2015, v. 7 n. 17, p. 1243-1249</td>
</tr>
<tr>
<td><strong>Issued Date</strong></td>
<td>2015</td>
</tr>
<tr>
<td><strong>URL</strong></td>
<td><a href="http://hdl.handle.net/10722/236437">http://hdl.handle.net/10722/236437</a></td>
</tr>
<tr>
<td><strong>Rights</strong></td>
<td>This work is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License.</td>
</tr>
</tbody>
</table>
Endoscopic submucosal dissection vs laparoscopic colorectal resection for early colorectal epithelial neoplasia

Sophie SF Hon, Simon SM Ng, Tiffany CL Wong, Philip WY Chiu, Tony WC Mak, WW Leung, Janet FY Lee

Sophie SF Hon, Simon SM Ng, Tiffany CL Wong, Philip WY Chiu, Tony WC Mak, WW Leung, Janet FY Lee, Department of Surgery, Prince of Wales Hospital, The Chinese University of Hong Kong, Shatin, Hong Kong, China

Author contributions: Hon SSF designed the study and drafted the manuscript; Ng SSM, Wong TCL and Chiu PWY designed study and data interpretation; Leung WW analysed data; Mak TWC and Lee JFY contributed to critical revision of the manuscript.

Informed consent statement: Consent from the participants was not obtained but the presented data are anonymized and risk of identification is low.

Conflict-of-interest statement: The authors have no conflicts of interest or financial conflicts to disclose.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/

Correspondence to: Dr. Sophie SF Hon, Department of Surgery, Prince of Wales Hospital, The Chinese University of Hong Kong, Shatin, NT, Hong Kong, China. honssf@surgery.cuhk.edu.hk
Telephone: +852-26321495
Fax: +852-26377974

Received: April 30, 2015
Peer-review started: May 8, 2015
First decision: June 2, 2015
Revised: July 10, 2015
Accepted: September 30, 2015
Article in press: October 9, 2015
Published online: November 25, 2015

Abstract

AIM: To compare the short term outcome of endoscopic submucosal dissection (ESD) with that of laparoscopic colorectal resection (LC) for the treatment of early colorectal epithelial neoplasms that are not amenable to conventional endoscopic removal.

METHODS: This was a retrospective cohort study. The clinical data of all consecutive patients who underwent ESD for endoscopically assessed benign lesions that were larger than 2 cm in diameter from 2009 to 2013 were collected. These patients were compared with a cohort of controls who underwent LC from 2005 to 2013. Lesions that were proven to be malignant by initial endoscopic biopsies were excluded. Mid and lower rectal lesions were not included because total mesorectal excision, which bears a more complicated postoperative course, is not indicated for lesions without histological proof of malignancy. Both ESD and LC were performed by the same surgical unit with a standardized technique. The patients were managed according to a standard protocol, and they were closely monitored for complications after the procedures. All hospital records were reviewed, and the following data were compared between the ESD and LC groups: patient demographics, size and location of the lesions, procedure time, short-term clinical outcomes and pathology results.

RESULTS: From 2005 to 2013, 65 patients who underwent ESD and 55 patients who underwent LC were included in this study. The two groups were similar in terms of sex ($P = 0.41$) and American Society of Anesthesiologist class ($P = 0.58$), although patients in the ESD group were slightly older (68.6 ± 9.4 vs 64.6 ± 9.9, $P = 0.03$). ESD could be accomplished with a shorter procedure time (113 ± 66 min vs 153 ± 43 min, $P < 0.01$) for lesions of comparable size (3.0 ± 1.2 cm vs 3.4 ± 1.4 cm, $P = 0.22$) and location (colon/rectum:
Laparoscopic colorectal resection (LC) is currently a widely accepted treatment for colorectal neoplasms that are deemed not amenable to endoscopic removal. However, LC carries an inherent complication rate of over 15%.[1,2] Therefore, one could argue that surgery may be too invasive or aggressive as a treatment for early colorectal neoplasms. The potential risks of laparoscopic resection may outweigh the estimated risk of lymph node metastasis if the neoplasms are not resected.[3-7]

On the contrary, endoscopic piecemeal removal of large sessile or flat polyps by conventional polypectomy or by endoscopic mucosal resection (EMR), although it is less invasive, is known to be associated with a high local recurrence rate of 14%-19.5%. Endoscopic submucosal dissection (ESD) is a novel technique that was originally developed in Japan more than 10 years ago. ESD was developed to achieve an en bloc mucosal resection with wider margins.[10-13] Currently, an increased number of endoscopists throughout the world have acquired this skill and have published promising outcomes of ESD.[14-19] The recent retrospective analysis reported by Kiriyama et al.[20] that compared ESD for colorectal intramucosal or slightly submucosal invasive cancers vs LC for T1 cancer demonstrated a lower complication rate in the ESD group. Another similar prospective study also compared ESD for adenoma or T1 cancer with less than SM-s (superficial submucosal invasion) vs LC for SM-d (deep submucosal invasion).[21] Until now, no worldwide consensus has been adopted as to whether the treatment of benign colorectal neoplasms with advanced endoscopic techniques (i.e., ESD) is superior to surgical approaches.[22] From the very beginning of the development of colorectal ESD, the procedure was performed primarily by gastroenterologists. No published data exists on the comparison of the clinical outcomes of ESD vs those of LC when both procedures were performed by the same group of surgeons. Surgeons who can perform both procedures may be in an advantageous position in that they can balance the risks and benefits of the endoscopic approach vs the surgical approach. Therefore, we performed a retrospective cohort study that aimed to compare ESD vs LC for endoscopically benign lesions that could not be adequately removed by conventional polypectomy. Case inclusion was based purely on the pre-operative/pre-procedure endoscopic findings. Although the difference in morbidities did not reach statistical significance, the absolute number of complications and the number of patients involved were much higher in the LC arm. The current study provided evidence that surgeons are capable of performing high-quality colorectal ESD procedures. We expect that the participation of the surgeons as well as the close collaboration with gastroenterologists will play a pivotal role in the formulation of a management plan for patients with early colorectal neoplasms.

**MATERIALS AND METHODS**

This was a retrospective cohort study conducted at Prince of Wales Hospital at, The Chinese University of Hong Kong. Since 2005, LC has been the gold standard surgical treatment for all colorectal lesions that are not amenable to endoscopic removal. Colorectal ESD was first established at our centre in 2008, and since that time, it has enriched the armamentarium of endoscopic interventions. Consecutive patients who underwent ESD or LC for early colorectal neoplasms (endoscopically benign lesions larger than 2 cm in diameter) from 2005 to 2013 were included. Lesions were excluded when endoscopic signs of massive submucosal invasion were present as evidenced by the existence of excavated/depressed morphology or...
Kudo’s pit pattern type V. Lesions proven to be malignant by initial endoscopic biopsies were also excluded. Mid and lower rectal lesions were not included because total mesorectal excision, which intrinsically bears a more complicated post-operative course and has a negative impact on gastrointestinal function, would not be offered to patients who were diagnosed with benign lesions by endoscopy. Nevertheless, the input of the patients would also influence the selection between ESD and LC because ESD was a relatively new procedure at that time.

Patients were instructed to eat a low residue diet two days before ESD or laparoscopic colectomy. They received four litres of polyethylene glycol solution as a mechanical bowel preparation on the day of ESD or one day before LC. Both ESD and LC were performed by surgeons who were capable of executing these procedures independently.

All hospital records were reviewed, and the following data were compared between the ESD and LC groups: patient demographics, size and location of the lesions, procedure time, short-term clinical outcomes and pathology result.

The ESD procedure and postoperative care

Our techniques for colorectal ESD have been previously reported. In short, all ESDs were performed when the patients were under conscious sedation after intravenous administration of midazolam and pethidine. Intravenous Buscopan was used if significant colonic spasms were encountered during the ESD procedure. All procedures were performed with a water-jet gastroscope or with a paediatric colonoscope with a transparent cap attached to the tip. Carbon dioxide insufflation was routinely used to reduce patient discomfort. The margins of the lesions were determined by either dye (0.4% indigo carmine spray) or digital (narrow band imaging) chromoendoscopy. Submucosal cushions were created by a mixture of normal saline, adrenaline, indigo-carmine and sodium hyaluronate. Circumferential mucosal incision and submucosal dissection were performed by dual knife or insulated tip knife (Olympus Medical System, Tokyo, Japan), depending on the location of the lesion and the preference of the endoscopists. Haemostasis after ESD was achieved by Coagrasper (Olympus Co. Ltd., Tokyo, Japan).

When perforations were encountered during the ESD procedure, they were immediately closed by endoscopic clips; otherwise, salvage surgery was arranged. For optimal procedures without significant bleeding, a diet would be resumed on the following day. Stable patients who managed to tolerate a full diet were discharged. For those patients with perforations that were managed by endoscopic clipping, they were kept nil per oral and monitored closely for signs of sepsis including fever, tachycardia, leukocytosis and peritonism. Depending on the clinical parameters, parenteral antibiotics were given and diet was gradually introduced. Salvage surgery was offered in cases of persistent or deteriorating sepsis.

All patients were encouraged to maintain mobility, and a diet was introduced gradually as tolerated. Patients were discharged when they could tolerate a full diet without signs of sepsis and the absence of rectal bleeding.

The LC procedure and postoperative care

All LCs were performed under general anaesthesia by the same group of colorectal surgeons, as described in our previous study. In short, the colon or rectum was mobilized laparoscopically from the lateral to the medial area. The isolated lymphovascular pedicles were then transected with either laparoscopic linear staplers or with self-locking plastic clips. One of the working ports was later extended for specimen retrieval. Extracorporeal anastomosis was fashioned for a right-sided resection, while intracorporeal stapled anastomosis was performed for a left-sided resection.

After surgery, the patients were allowed to ingest oral fluid on day one. Diet was resumed gradually during the days following the surgery and depended on the progression of the patients. All patients received regular physiotherapy and were mobilized as soon as possible after surgery. Pain control was achieved by either regular analgesics or by patient-controlled analgesia. Ambulatory patients were discharged if they could tolerate a full diet with no signs of sepsis.

Histological assessment

All ESD specimens were mounted on a foam board for pathological examination by a designated pathologist. Deep and peripheral margins, cellular differentiation as well as the depth of submucosal invasion were recorded. R0 resection was defined as a complete en bloc resection with deep and circumferential margins that were free of adenomatous proliferation or dysplasia. Colectomy specimens were evaluated after fixation in 10% formalin and after staining with haematoxylin and eosin. Macroscopic and microscopic examinations for histological type, depth of invasion, lymph node status and resection margins were performed. Malignant lesions were classified according to the AJCC Cancer Staging Manual, 7th Edition (2010).

Outcomes measurement

In regards to the short-term clinical outcomes, we studied the procedure time, the time to resume diet, the time to full ambulation, the duration of the total hospital stay and the complication rate.

Lesions that were located in the colon and at the rectosigmoid junction were defined as “colon”, while lesions in the upper rectum were defined as “rectum”.

Complications were defined as any event that required re-intervention, re-operation, re-admission or a prolonged hospital stay (namely, Clavien-Dindo Grade II or above). Bleeding from the ESD procedure was defined as any bleeding episodes after ESD that warranted intravascular transfusions or required re-intervention.
Hon SSF et al. Endoscopic submucosal dissection vs laparoscopic colectomy

Table 1 Demographic background

<table>
<thead>
<tr>
<th></th>
<th>Lap colectomy</th>
<th>ESD</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>55</td>
<td>65</td>
<td>0.03</td>
</tr>
<tr>
<td>Age (yr), mean ± SD</td>
<td>64.6 ± 9.9</td>
<td>68.6 ± 9.4</td>
<td>0.07</td>
</tr>
<tr>
<td>Sex</td>
<td>Female: 27</td>
<td>Female: 27</td>
<td>0.41</td>
</tr>
<tr>
<td></td>
<td>Male: 28</td>
<td>Male: 38</td>
<td></td>
</tr>
<tr>
<td>ASA</td>
<td>&lt; 3 vs ≥ 3</td>
<td>&lt; 3 vs ≥ 3</td>
<td>0.58</td>
</tr>
<tr>
<td></td>
<td>3.4 ± 1.4</td>
<td>3.0 ± 1.2</td>
<td></td>
</tr>
<tr>
<td>Size of lesion (cm), mean ± SD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Location of lesion</td>
<td>Colon: 52</td>
<td>Colon: 59</td>
<td>0.43</td>
</tr>
<tr>
<td></td>
<td>Rectum: 3</td>
<td>Rectum: 6</td>
<td></td>
</tr>
</tbody>
</table>

ASA: American Society of Anaesthesiology; ESD: Endoscopic submucosal dissection.

Table 2 Comparisons of the short-term outcome

<table>
<thead>
<tr>
<th></th>
<th>Lap colectomy</th>
<th>ESD</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>OT/procedure time (min), mean ± SD</td>
<td>153 ± 43</td>
<td>113 ± 66</td>
<td>0.000</td>
</tr>
<tr>
<td>Post-op stay (d), median (range)</td>
<td>6 (4-11)</td>
<td>3 (1-13)</td>
<td>0.000</td>
</tr>
<tr>
<td>Days to diet, median (range)</td>
<td>4 (1-13)</td>
<td>2 (0-5)</td>
<td>0.000</td>
</tr>
<tr>
<td>Short-term complications</td>
<td>13/55 (23.6%)</td>
<td>7/65 (10.8%)</td>
<td>0.06</td>
</tr>
<tr>
<td>Pathology</td>
<td>Benign: 39</td>
<td>Benign: 56</td>
<td>0.04</td>
</tr>
<tr>
<td></td>
<td>T1: 16</td>
<td>T1: 9</td>
<td></td>
</tr>
</tbody>
</table>

ESD: Endoscopic submucosal dissection; OT: Operation time.

RESULTS

From 2005 to 2013, 55 patients who underwent LC and 65 patients who underwent ESD were included in this study. The mean age of the patients in the ESD group was slightly higher than that of the patients in the LC group. The two groups shared comparable sex and ASA class distributions (Table 1).

No statistically significant differences were observed in terms of lesion size or location, yet ESD could be accomplished with a significantly shorter procedure time (113 ± 66 min vs 153 ± 43 min, P < 0.01) and a faster recovery course, as illustrated by earlier resumption of a full diet (2 d vs 4 d, P = 0.01) and a shorter hospital stay (3 d vs 6 d, P < 0.01) (Table 2).

The overall short-term complication rate for ESD and LC was 10.8% and 23.6%, respectively. Although we could not demonstrate a significant difference between the two groups (P = 0.06), the ESD group exhibited a trend towards a lower short-term complication rate. In the LC arm, a total of 22 complications occurred in 13 patients (Table 3). These included 1 anastomotic leak, 1 mechanical small bowel obstruction, which required re-operation, 6 wound infections, 1 chest infection, 4 urinary tract infections, 1 acute urine retention, 6 cases of prolonged ileus, 1 deep vein thrombosis, and 1 mental confusion. A total of 7 complications occurred in the ESD arm, including 5 perforations and 2 bleeding episodes. The remainder of the patients in the ESD arm experienced a smooth intra- and post-procedure course without complications. All of the perforations were observed during the procedure and were successfully managed by endoscopic clipping. Therefore, no emergency surgical intervention was needed. One of the bleeding episodes was successfully stopped during the procedure, and blood transfusion was required. Unfortunately, the other incident was encountered during the removal of a caecal lateral spreading tumour (LST). As a result of malfunction in the water-jet, a clear endoscopic view could not be achieved for safe haemostasis and dissection. Hence, the procedure was abandoned and was followed by emergency LC. The patient was discharged home 4 d after surgery. No delayed perforation, bleeding or other post-procedure complications were recorded in the ESD arm (Table 4).

En bloc resection was achieved in 81.5% (53/65) of the ESD procedures. For the remaining 12 lesions, 6 were completely removed by piecemeal EMR. Endoscopic removal had to be abandoned for the other six lesions due to instrumental failure in one case and the presence of dense adhesions in five cases. Amongst the 5 lesions that harboured these dense adhesions, 3 were confirmed T1 adenocarcinomas.

In this study, histological analysis revealed the presence of T1 adenocarcinomas in 25 lesions (LC: 16 and ESD: 9). The proportion of invasive neoplasms was significantly higher in the LC arm (29.1% vs 15.3%, P = 0.04). En bloc ESD resection was successfully achieved in 4 of 9 malignant lesions, and all four of these patients were subsequently managed according to the level of submucosal (sm) invasion and other associated histological features. Although salvage surgery was offered to the two patients with sm2 lesions, they both rejected this procedure. On the contrary, one patient with an sm3 lesion agreed to undergo LC, and the pathology of the resected specimen showed no residual primary tumour; however, one metastatic lymph node was identified. The remaining patient with an sm1 lesion was put under close surveillance in light of an adequate resection margin and the absence of lymphovascular permeation. ESD was abandoned in 3 of 9 malignant lesions due to dense submucosal adhesion, of which 2 were salvaged by LC and 1 by TEO (transanal endoscopic operation).
Piecemeal resection was performed in the other 2 of 9 lesions, of which one refused salvage surgery and the other one accepted salvage LC.

**DISCUSSION**

Since the development of colorectal ESD, its feasibility, safety and oncological outcome have been reported in numerous contemporary studies. Currently, nearly 3000 colorectal ESDs are performed each year in Japan. The Japanese healthcare insurance system has also approved a reimbursement scheme for colorectal ESD. On the contrary, the adoption rate of ESD is variable in the rest of the world, especially among surgical societies. To explain this, two potential hurdles have been identified. First, the technique of LC had already been widely practised and supported by a high level of evidence at the time when colorectal ESD was introduced outside of Japan. Second, the volume of cases did not justify a large number of endoscopists having to learn and master the technique of ESD. Moreover, current literature that directly compares LC vs ESD for early colorectal neoplasms is not available. Two recent studies compared ESD for mucosal or slight submucosal invasive lesions vs LC for T1/deep submucosal invasive lesions, but the pathological nature of the two comparative groups was different.

This is a retrospective cohort study that compared ESD vs LC for endoscopically confirmed benign lesions that could not be adequately removed by conventional polypectomy. Case inclusion was based purely on the pre-operative/pre-procedure endoscopic findings, and no crossover of abandoned ESD to LC occurred. The results of this study suggested that ESD was superior to LC with respect to short-term outcomes and that ESD leads to a faster recovery. Despite the fact that perforation and bleeding did occur in the ESD arm, all but one of these events could be managed endoscopically. The post-operative course of the only patient who underwent salvage surgery for complications was also uneventful. Although the difference in morbidities did not reach statistical significance, the absolute number of complications and the number of patients involved are much higher in the LC arm.

Moreover, all ESD procedures were performed when the patients were under conscious sedation without general anaesthesia. This definitely avoided the risks of general anaesthesia and post-operative wound pain. Almost immediate mobilization was feasible once the sedative effect subsided. Therefore, we believe that ESD might be more reasonable and acceptable for patients with early colorectal neoplasia or LSTs.

The ESD perforation rate in this study was 7.7%, which was comparable with quoted figures in the literature. In a recent meta-analysis, the highest reported perforation rate was 12% (18), and most of the reported rates in published series were well below 10% (27). Although these perforation rates might be considered higher than those at some of the high-volume Japanese centres, they were comparable with large series that have been conducted outside of Japan (28,31). This cohort study only reflected the early phase of our learning curve, and we expect a further reduction in morbidity in the future. Due to the increasing popularity of screening colonoscopy and image-enhanced endoscopy, a greater number of early colorectal lesions might be detected. Therefore, we expect a higher ESD throughput and an improved performance at our centre.

In reality, whether an endoscopically assessed benign lesion is subjected to ESD or colectomy depends to a large extent on who detects the lesion. For instance, if a gastroenterologist who is capable of performing ESD detects an LST, then an ESD procedure might be attempted. Likewise, if the same lesion is detected by a surgeon who does not possess the skills to perform ESD, then colectomy would be offered instead. In our locality, it is rather unique that surgeons actively participate in advanced diagnostic and therapeutic endoscopies. At our centre, we have a group of surgeons who have acquired the skills to perform both LC and colorectal ESD, and who can confidently counsel patients and offer them both options (ESD vs LC). One can also comprehensively balance the risks and benefits between conservative management vs salvage surgery for histologically confirmed malignant lesions that are removed by ESD. The current study provided evidence that surgeons are capable of performing high-quality colorectal ESD. We expect that the participation of the surgeons as well as the close collaboration with gastroenterologists will pay a pivotal role in the formulation of a management plan for colorectal neoplasia.

---

**Table 3** Complications of laparoscopic colectomy (22 events in 13 patients)

<table>
<thead>
<tr>
<th>Complication</th>
<th>Number of complications</th>
<th>Surgical intervention required</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anastomotic leak</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Mechanical small bowel obstruction</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Wound infection</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Chest infection</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Urinary retention</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Ileus</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Deep vein thrombosis</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Confusion</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

**Table 4** Performance indicators of endoscopic submucosal dissection

<table>
<thead>
<tr>
<th>Indicator</th>
<th>n</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>En bloc resection</td>
<td>53</td>
<td>81.5</td>
</tr>
<tr>
<td>R0 resection</td>
<td>47</td>
<td>72.3</td>
</tr>
<tr>
<td>Perforation</td>
<td>5</td>
<td>7.7</td>
</tr>
<tr>
<td>bleeding</td>
<td>2</td>
<td>3.1</td>
</tr>
</tbody>
</table>

No other complication apart from perforation and bleeding were observed.
patients with early colorectal neoplasms.

The major limitation of the current study was its retrospective nature that extended through a period of eight years, during which time major advances in both laparoscopic and endoscopic technology occurred. Most of the LC cases were recruited prior to the availability of image-enhanced endoscopy (2005-2008), when endoscopic diagnoses were less accurate. This explained why patients in the LC arm had more malignant lesions, which was also a major bias of the current study. During the past few years, we have introduced enhanced recovery protocols in our unit, and thus the same LC group may experience a faster recovery and potentially fewer morbidities. To address these biases, a randomized controlled trial is necessary to provide a higher level of evidence to compare these two intervention modalities. We are currently awaiting the results of our randomized controlled trial.

In conclusion, by a comparison of LC and ESD performed by the same group of surgeons for the treatment of early colorectal neoplasms, ESD produced better short-term clinical outcomes with respect to a shorter procedure time and an earlier recovery. Therefore, ESD may be superior to LC for the treatment of this specific type of colorectal lesion.

REFERENCES


Hon SS et al. Endoscopic submucosal dissection vs laparoscopic colectomy.


P- Reviewer: Matsumoto S, Tsuji Y
S- Editor: Yu J
L- Editor: A
E- Editor: Jiao XK