

Manuscript Type: THERAPEUTIC ADVANCES

Colorectal ESD from a western perspective: Today's promises. Future challenges.

1.) when comparing ESD to TEM and laparoscopic surgery, I suggest adding some information of typical hospital length-of-stay in Western centers. In the USA, 3 days hospital stays with laparoscopic partial colectomy and < 24 hour stays with TEM are now commonplace. This is in contrast to Japan where a week or longer is common, and may alter the approach to treatment.

A new paragraph has been added in the TEM section.

“Regarding hospital stay with TEM, this outcome may vary significantly across centers. Thus, some authors have reported a median hospital stay of 2-3 days [104-107], while other studies suggest even shorter stays and have reported a 24 hour discharging policy [108]. To our knowledge, prospective direct comparisons between TEM and ESD that address the question of superiority in terms of length of hospital stay have yet to be published.”

A new paragraph has been added in the LACS section.

“In terms of hospital stay, five days or longer on LACS groups are common in Japanese studies. However, other studies have reported shorter periods when an elective surgery has been performed, ranging from 3 [52] to 6 days [89-91]”.

2.) For ESD, it's important to discuss the minimum hospital stay required due to the risk of delayed perforation. I recommend adding more discussion on this topic, and some conclusions regarding what the authors think is a reasonable post-procedure stay.

A new paragraph has been added in Section 4: OUTCOMES IN ASIAN AND IN EUROPEAN COUNTRIES.

“Since ESD is accompanied by risk of delayed perforation and bleeding the postoperative course needs to be monitored carefully. However, no recommendations have been established for patient discharge after the procedure. Some Japanese authors have suggested a 5-day hospital stay for ESD [73]. In Korea and some European countries, duration of the hospital stay is 2 – 3 days in most cases unless complications develop [16, 72]. Recently, a Japanese group has published a clinical pathway with the aim of shortening hospital stay after ESD. The authors concluded in the study that discharge may be possible 3 days after ESD when no

abnormalities are noted during ESD or on post-ESD day 1 [74]. In our center, the length of the hospital stay is typically 3 days when no complications are observed. No delayed perforations have been identified after those 3 days in our experience; indeed, this complication is more likely to happen during the first 24 hours after the procedure.”

3.) discussion of alternative approaches to recurrent adenomas in the colon. Perhaps some data comparing ESD to repeat EMR, or maybe even underwater EMR.

The following paragraphs have been added in the EMR section:

“The endoscopic resection of recurrent adenomas is another matter of concern. Although ESD may be suitable for use in endoscopic salvage procedures for recurrent lesions, performing this procedure is extremely difficult because of the development of submucosal fibrosis caused by previous resection. For this reason, in the Western world, the most commonly attempted endoscopic procedure for recurrent adenomas after EMR is to repeat this treatment although fibrosis after a previous EMR often prevents lifting of the lesion after submucosal injection and causes the snare to slip off the tumor. There are very limited published data on the results for this strategy, with more than 10% of the patients needing surgery in this scenario [7].

In a retrospective case series that included 67 cases of a second endoscopic resection for recurrent neoplasias, ESD achieved a 56% *en bloc* resections when compared with a 39% in the EMR group. Both of these results are lower than expected for primary colorectal tumors [86]. In the other hand, another study observed that 27 out of 28 patients were successfully treated using ESD for residual or recurrent colorectal of tumors [67]. However, in the western world, the most commonly attempted endoscopic procedure for recurrent adenomas after EMR is repeat this treatment although there are very limited published data on the results for these strategy, with more than 10% of the patients needing surgery [7].

More recently, underwater EMR (UEMR) has been evaluated for the treatment of these recurrences. When water is used rather than gas to distend the lumen, the mucosa and submucosa involute, whereas the muscle layer does not, and there is no need for submucosal injection. Thus, you can snare the tumor easier than with conventional EMR. In a retrospective study, the *en bloc* resection rate and endoscopic complete removal rate were higher in the UEMR group than in the EMR group and these differences were statistically significant. In addition, APC ablation of residual tumor was lower in the UEMR group[87]. Although the study had several limitations, UEMR appears to be a promising technique for salvage endoscopic treatment of recurrent adenomas after a previous EMR.”