



## EDITORIAL

## Endoscopic Submucosal Dissection in the Treatment of Gastrointestinal Superficial Lesions: Follow the Guidelines!



### Disseccão Endoscópica da Submucosa no Tratamento de Lesões Superficiais Gastrointestinais: Sigamos as Recomendações!

Pedro Pimentel-Nunes<sup>a,b,\*</sup>, Mário Dinis-Ribeiro<sup>a,b</sup>

<sup>a</sup> Gastroenterology Department, Portuguese Oncology Institute of Porto, Porto, Portugal

<sup>b</sup> Center for Research in Health Technologies and Information Systems (CINTESIS), Faculty of Medicine, Porto, Portugal

The detection of early gastrointestinal neoplastic lesions commonly known as superficial lesions is increasing.<sup>1</sup> Even though current oncological Western guidelines still consider surgery as the gold standard of treatment, endoscopic resection can cure a substantial number of these patients. In fact Japanese Cancer guidelines consider endoscopic approach as the preferred approach for these lesions, as long as they are considered endoscopically resectable.<sup>2</sup> The main reason for this is that endoscopic treatment is considered less invasive and potentially less disturbing of the quality of life of the patients when compared to alternative treatments. Moreover, several and large Eastern series as well as recent Western series confirm these aspects showing that, in fact, endoscopic resection can cure more than 80–85% of these lesions and that in the worse scenario the endoscopic resected specimen can be the best staging tool of the neoplasia with a good safety profile.<sup>3</sup>

Endoscopic resection of superficial lesions was initially performed by different techniques of endoscopic mucosal resection (EMR). However, it was soon apparent that EMR could not achieve en bloc complete resection (R0) of lesions larger than 15–20 mm or nonlifting lesions.<sup>3</sup> This can hamper a correct histopathological evaluation of the neoplasia, not allowing a complete assumption of a curative resection and in some cases it could send to surgery some patients

that in fact would not need surgery. To overcome these EMR limitations endoscopic submucosal dissection (ESD) using several and different devices was developed. Even though ESD is technically demanding and with a longer learning curve when compared to standard EMR, it rapidly gained wide popularity among gastroenterologists. In fact, in the East ESD is nowadays extensively used with excellent results and safety profile and in Western countries it is being increasingly reported. However, even though meta-analysis clearly show that the rates of en bloc R0 resection are much higher and consequently the rates of recurrence much lower, even for lesions smaller than 10 mm, the safety profile appears to be worse when compared to EMR.<sup>3</sup> Moreover, there are no randomized trials comparing ESD to EMR or on the other extreme comparing ESD to surgery. In fact, long term comparative series of these techniques, all of them retrospective, do not show differences in survival.<sup>4–7</sup>

For all these reasons the European Society of Gastrointestinal endoscopy (ESGE) recently developed guidelines concerning the role of ESD in the treatment of gastrointestinal superficial lesions.<sup>8</sup> Concerning the pre-treatment evaluation of these lesions it was consensual that after biopsies with dysplasia/carcinoma these patients should be sent to a referral centre to perform a high quality endoscopy with chromoendoscopy (for example virtual chromoendoscopy with NBI) by an experienced endoscopist in order to establish the feasibility of endoscopic resection, delimitation of the lesion and decision of the best therapeutic technique. As a general rule no additional complementary procedure like

\* Corresponding author.

E-mail address: [pedronunesml@gmail.com](mailto:pedronunesml@gmail.com) (P. Pimentel-Nunes).

endoscopic ultrasound or CT is recommended previously to endoscopic treatment.

ESD was considered the first line treatment for esophagus squamous cell carcinoma, mainly because the curative criteria are too restrict and a piecemeal resection may hamper significantly the management of these patients, and in the stomach where ESD is technically easier and the safety profile is not significantly different when comparing to EMR. In the duodenum ESGE recommended against performing ESD mainly because of the prohibitive rate of perforations. In the colon it was difficult to obtain a consensus or to achieve a straight indication for ESD. ESGE recognized that EMR (en bloc or piecemeal) is able to treat most of colorectal superficial lesions with a better safety profile when compared to ESD even though with a high recurrence rate (that can be treated by another EMR or argon plasma). Nevertheless, ESGE considered that a depressed, irregular or non-granular pattern particularly in lesions larger than 20 mm should be a consideration for ESD. However, even for this type of lesion, the recommendation for ESD was not absolute because some consider that colectomy is a safe and more definitive treatment when compared to ESD. Even in the rectum ESD was not an absolute indication for this type of lesions since video transanal surgical approaches are also a technique with good results presented in the literature. So, it appears that for colorectal superficial lesions further prospective studies should compare ESD to EMR (for lesions less advanced) or to surgical approaches (for lesions suspicious of submucosal invasion) before absolute indications for ESD can be made.

ESGE also discussed and made some recommendations regarding training (appendix of the guidelines). ESD should only be attempted by endoscopists already experienced in therapeutic endoscopy (namely EMR) and before starting ESD in humans they should observe experts and have enough practice with animal models. Performance of ESD in humans should start carefully with small lesions, first in the stomach (ideally in the antrum) or rectum, then in the esophagus and only after expertise in these areas, a colonic ESD should be tried (after proper discussion with the patient of the risk benefit relation when comparing to surgery). Unfortunately, many endoscopists without enough practice are starting to perform ESD and sometimes without clear indications and in difficult areas (for instance ESD for granular lesions in the colon). Moreover they do not keep records of the procedures nor do they know the results of the ESD they are doing. Indeed, ESGE advise that "centers performing ESD should keep records on all referred patients, and for those who finally undergo ESD, records should be kept on rates of en bloc and R0 resections, on adverse events rates, and on follow-up".

In this line of thoughts we applaud the manuscript by Rodrigues et al. published in this issue of the GE.<sup>9</sup> It represents the second ESD series in Portuguese centers published in GE, and it is the first one considering several organs.<sup>10</sup> First of all, in the absence of European indications (now published) the authors selected the lesions based on Japanese and International criteria reflecting precise criteria in the selection of the lesions for ESD. Secondly, the endoscopist performing ESD presented his training and all the steps of training were fulfilled according to European guidelines. Finally, they kept records of the procedures and they now present their results. So, all the fundamental principles

when starting a new therapeutic technique were accomplished by the authors.

Concerning the results and even though it is a small retrospective series with only 34 lesions included some considerations can be made. The results of gastric ESD (n = 18), considered the easiest area for ESD, were similar to the results presented in the literature including Portuguese ones, with en bloc R0 resection rates approaching 90%. Moreover, no significant complication was observed after gastric ESD. In the rectum (n = 15) the results are somewhat worse with 73% of en bloc and only 60% R0 resection rates. However, most Western series also present lower rates of en bloc R0 resection when comparing to Eastern ones and with a worse safety profile, which was not the case in this series since there was no perforation, even though with a 20% rate of bleeding which was slightly higher to other series. Nevertheless, all the hemorrhage was considered minor and easily controlled by endoscopy. In the esophagus no consideration can be made since only one lesion was resected by ESD. The authors did not perform any duodenal or colonic ESD and, for the reasons previously stated, it was a good decision since there is no clear recommendation for performing ESD in these areas, particularly in Western countries. The low rate of recurrence is also remarkable with only one recurrence after rectum ESD (7%), however, the short-follow up of the patients (mean of 13–16 months) does not allow to make any other consideration, namely regarding survival.

Altogether, ESD is probably the best endoscopic therapy for gastrointestinal superficial lesions but it should only be performed by proper trained endoscopists in referral centers. European recommendations should be followed in order to minimize the risks for patients. Similarly to what was made by Rodrigues J et al., centers who are performing ESD should keep records of all the ESDs that have been done in order to present rates of en bloc R0 resection and adverse events of the technique. Only fulfilling these steps we can present our results to our patients allowing them to make a conscious decision about their treatment and, in this way, we can expect to better treat our patients.

## References

1. Lambert R. Endoscopy in screening for digestive cancer. *World J Gastrointest Endos.* 2012;4:518–25.
2. Japanese Gastric Cancer Association. Japanese gastric cancer treatment guidelines 2010 (ver. 3). *Gastric Cancer.* 2011;14:113–23.
3. Cao Y, Liao C, Tan A, Gao Y, Mo Z, Gao F. Meta-analysis of endoscopic submucosal dissection versus endoscopic mucosal resection for tumors of the gastrointestinal tract. *Endoscopy.* 2009;41:751–7.
4. Das A, Singh V, Fleischer DE, Sharma VK. A comparison of endoscopic treatment and surgery in early esophageal cancer: an analysis of surveillance epidemiology and end results data. *Am J Gastroenterol.* 2008;103:1340–5.
5. Tanabe S, Ishido K, Higuchi K, Sasaki T, Katada C, Azuma M, et al. Long-term outcomes of endoscopic submucosal dissection for early gastric cancer: a retrospective comparison with conventional endoscopic resection in a single center. *Gastric Cancer.* 2014;17:130–6.
6. Pimentel-Nunes P, Mourao F, Veloso N, Afonso LP, Jacome M, Moreira-Dias L, et al. Long-term follow-up after endoscopic

- resection of gastric superficial neoplastic lesions in Portugal. *Endoscopy*. 2014;46:933–40.
7. Chiu PW, Teoh AY, To KF, Wong SK, Liu SY, Lam CC, et al. Endoscopic submucosal dissection (ESD) compared with gastrectomy for treatment of early gastric neoplasia: a retrospective cohort study. *Surg Endoscopy*. 2012;26:3584–91.
  8. Pimentel-Nunes P, Dinis-Ribeiro M, Ponchon T, Repici A, Vieth M, De Ceglie A, et al. Endoscopic submucosal dissection: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. *Endoscopy*. 2015;47:829–54.
  9. Rodrigues J, Carmo J, Carvalho L. Endoscopic submucosal dissection for gastrointestinal superficial lesions: initial experience in a single Portuguese center. *GE Port J Gastroenterol*. 2015;22:192–7.
  10. Ribeiro-Mourão F, Veloso N, Dinis-Ribeiro M, Pimentel-Nunes P. Endoscopic submucosal dissection of gastric superficial lesions: predictors for time of procedure in a Portuguese Center. *GE Port J Gastroenterol*. 2015;22:52–60.