Endoscopic submucosal dissection (ESD): still a matter for debate or a gold standard technique in both Western and Eastern countries?

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Endoscopic submucosal dissection (ESD) was developed to make possible the en bloc removal of large, flat, superficial lesions of the gastrointestinal tract, and reports on its efficiency were first published more than 25 years ago [1,2]. In Eastern countries, this technique became the gold standard for the treatment of early gastric cancer. Since then, indications for the method have been expanded to include other structures, such as the esophagus and colon, and other types of lesions, such as submucosal tumors. In well-validated indications, assessments of both the short- and long-term efficacy of ESD, along with safety and recurrence rates, have proved its superiority to all other therapeutic modalities, including ablation techniques, endoscopic mucosal resection (EMR), and surgery. Recent studies have confirmed that ESD is superior to EMR in terms of higher rates of en bloc resection and histologically proven complete resection of early gastrointestinal neoplasia, along with resultant lower rates of recurrence [3,4].

In the Western world, the role of ESD is still a subject of debate, and most editorials and reviews emphasize the associated difficulties, concerns, and caveats [5]. At many conferences, the "pros and cons" of the use of ESD continue to be debated [6]. Evidence of its clinical value is still limited and based primarily on data from Japan. Such data may not be directly applicable to Europe, where the outcome of ESD may be innately less favorable because of limited Western expertise in this challenging technique. I personally find this continuing debate, and the obstacles that still prevent ESD from being adopted as a "gold standard," quite surprising. From the early beginnings of ESD, I have felt that it would revolutionize endoscopy in the same way that both endoscopic ultrasonography (EUS) and natural orifice transluminal endoscopic surgery (NOTES) have modified our vision of current and future endoscopic therapy. EUS enables us to look in and through the digestive wall, and NOTES has increased our confidence in accessing the peritoneal and mediastinal spaces. The ESD technique has created another bridge between endoscopy and surgery, providing interventional endoscopists with access to "surgical" and "oncologic" values, such as R0 resection and complete remission of cancer. Furthermore, ESD has improved our technical skills in hemorrhage control and enabled the development of new tools and techniques, such as the tunneling methods of peroral endoscopic myotomy (POEM) in achalasia.

The Western ESD debate centers primarily on two issues: concern regarding training and the "well-validated" appropriateness of piecemeal EMR. Although piecemeal resection is no longer considered suitable for early gastric cancer (including carcinomas of the esophagogastric junction) or esophageal squamous carcinoma, it is still considered appropriate in other contexts, such as Barrett's and colorectal neoplasias. Used in these conditions, en bloc and histologically proven complete resection of early gastrointestinal neoplasia has exerted only a minor effect on clinical outcome. The typical issues associated with EMR – incomplete resection in these locations, along with higher recurrence rates – have been shown to be "easily" managed by early follow-up endoscopies and endoscopic re-treatment [7,8].

Evidence of the clinical value of ESD is indeed still limited and based primarily on Japanese data, which cannot be directly extrapolated to our countries [9]. The level of evidence demonstrating the superiority of ESD over EMR in terms of clinical outcome is even weaker in the context of Barrett's neoplasia. In addition, the contribution offered by Komeda and colleagues to this debate [10] further illustrates that the superiority of ESD in this location will be difficult to prove. Their literature review included a total of 16 studies: 10 EMR studies originating from Western countries and 6 ESD studies from Japan, published be-

tween January 2006 and May 2013. Their paper concluded that EMR, and more specifically the multiband technique, is as effective as ESD for managing early Barrett's neoplasia or esophagogastric junction neoplasia when outcomes in terms of recurrence and complication rates are compared. Recurrence rates were slightly higher in the EMR group than in the ESD group, although the difference was not statistically significant: 2.6% (10 of 380) for EMR versus 0.7% (1 of 133) for ESD. More importantly, all recurrences in the EMR group were managed by additional endoscopic resections. The risks of delayed bleeding, perforation, and stricture were similar in both groups. The authors acknowledged the following limitations of their literature review: all studies included were limited by the constraints of a nonrandomized design involving a nonconcurrent comparison group, and long-term data were lacking for both sets of studies.

Further studies involving randomized, controlled trials of EMR versus ESD in early Barrett's neoplasia are therefore required to determine the respective indications for each technique. Recent guidelines have been drawn up attempting to define the indications for ESD in Barrett's esophagus with superficial adenocarcinoma. The Sociedad Española de Endoscopia Digestiva (SEED) provides the following recommendations: ESD is indicated in lesions exceeding 20 mm in size with high-grade dysplasia, carcinoma in situ, or invasive carcinoma up to m2 or m3. ESD may be indicated in patients with a high surgical risk and invasive adenocarcinoma affecting the first third (sm1 = 500 µm) of the submucosal layer (level of evidence, 2+; grade of recommendation, C) [11]. The preferred treatment choice in the Western world (EMR vs. ESD vs. surgery) should be based on lesion size (>15 or 20 mm), degree of fibrosis with poorly lifting lesions, and suspicion of invasion of the submucosal layer.

With regard to the issue of training, should a technique that requires more training and expertise than others be underused, or should it be developed in specialized, large-volume centers? ESD is a complex and demanding technique that requires extensive training comprising a comprehensive study of ESD basics, the observation of live cases, and the performance of initial interventions in animal models, ideally under expert supervision [12]. However, the issue of training in endoscopy is not limited to the ESD technique; it is relevant to all advanced interventional endoscopic procedures. Training for endoscopic retrograde cholangiopancreatography (ERCP) and EUS is also a lengthy process, and true mastery of these methods can take 2 to 5 years of practice. Is training for ERCP and EUS any more easily accessible, then? Moreover, once the necessary experience has been acquired, will the case load per endoscopist really be sufficient to maintain competence? More and more centers are now routinely performing ESD, reflected by an increased number of papers on and awareness of the benefits of the technique [13–16]. Our population is getting older, and more cases of superficial cancers and other ESD indications are being diagnosed now than ever before. It seems to me that ESD is a good example of an advanced endoscopic technique that should not remain underutilized; rather, it should be performed in expert centers providing optimal care for selected patients.

Given its great potential benefits, ESD is certain to become the method of choice for the local treatment of selected forms of neoplasia in Western countries, once we are able to acquire sufficient expertise. This goal has now been all but reached with the help of technical improvements and structured training. Some indications, such as squamous cell carcinoma and early gastric cancer, are now fully accepted, even in our Western world, whereas others, such as Barrett's tumors and colorectal laterally spreading tumors, still require further studies. In Barrett's neoplasia, however, ESD does already appear to be justified in selected cases, such as neoplastic lesions that exceed 15 mm, are difficult to remove by EMR (e.g., because of submucosal fibrosis), or are suspected of submucosal invasion, thus requiring complete histologic evaluation. In these indications, there is little chance that prospective, randomized trials will be undertaken to compare ESD with EMR, given that most currently practicing interventional endoscopists would never remove these lesions in a piecemeal fashion, even in our part of the world.

Competing interests: None

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