

Endoscopic therapies are ever-changing strategies and never-ending challenges for gastroenterological neoplasia and the refractory conditions

Endoscopic mucosal resection (EMR) is accepted as a treatment of choice for early gastrointestinal (GI) cancers and tumors. Nevertheless, snaring-based procedure of the EMR is limited in the lesion size and is not reliable for lesions with ulcer findings. Endoscopic submucosal dissection (ESD) has been developed as an endoluminal therapeutic technique for superficial GI neoplasia. ESD has the advantage over EMR with respect to curative resection, removing even extensive GI tumors or ulcerated gastric cancer in the early stage in an *en bloc* manner. ESD allows precise histological assessment of the resected one-piece specimens in order to guide further management and to stratify a patient's risk for developing metastasis. As a result, it may prevent residual disease and local recurrence following treatment (1,2). Nowadays, ESD has been covered by health insurance for GI superficial neoplasia, mainly for mucosal cancers. Although the clinical results of ESD are promising, most studies on clinical outcomes of ESD were conducted at selected and advanced institutes. ESD requires endoscopic skill and sufficient experience and it might be still associated with risks of procedure-related complications such as bleeding and perforation for esophageal and colonic lesions due to their luminal thinness (3,4). Using diagnosis procedure combination (DPC), which is a nationwide database in Japan and can include about 50% of all inpatient admissions to acute-care hospitals, complications after esophageal ESD was documented. Based on 12,899 esophageal ESD procedures in 699 hospitals from 1 July 2007 to 31 March 2013, we identified 422 (3.3%) patients with perforation and perforation-related disorders following esophageal ESD. Among these 422 patients, 7 (1.7%) received open thoracotomy for treatment of esophageal perforation. There was a linear association between lower hospital volume and a higher rate of perforation and perforation-related disorders following esophageal ESD. Again, based on 7,567 colorectal ESDs in 421 hospitals during the 1 April 2012 to 31 March 2013, there was a linear association between lower hospital volume and higher rate of postoperative bleeding perforation occurred in 13 (0.2%) patients, reaching insignificance among the diverse volume hospitals. Esophageal stricture following semicircular or complete circular esophageal ESD was relatively frequent even when treated by multiple pre-emptive endoscopic balloon dilation. Endoscopic triamcinolone injection, temporal stenting and innovative transplantation of autologous tissue-engineered epithelial cell sheets have shown promising results for the prevention of luminal stricture following semicircular esophageal ESD. In cases of circumferential ESD, however, giving oral prednisolone can offer a unique treatment option for the prevention of post-procedural stricture of the esophagus (5). The luminal strictures of the alimentary tract are still intractable in the other gastroenterological diseases such as Crohn's disease. In this regard, Suzuki *et al.* performed a promising phase 1 clinical study of siRNA targeting carbohydrate sulphotransferase 15 (CHST15) in Crohn's disease patients. CHST15 is a specific enzyme biosynthesizing chondroitin sulphate E that binds various pathogenic mediators and is known to create local fibrotic lesions (6). Using the CHST15 siRNA, esophageal post-ESD stricture formation can be also alleviated via repression of fibrosis.

Duodenal ESD has not yet reached the recommendable measure for the endoscopic treatment of duodenal tumors (7). To reduce the incidence of complications as much as possible, the cases of possible indication of duodenal ESD should be collected to such specific institutions with advanced techniques and experiences. Nevertheless, it seems difficult to prevent the intraoperative perforation singly by the progress of ESD techniques or related devices, implying the necessity of a fundamental change of the therapeutic method. From the perspective of a combined treatment, the further radical progress of laparoscopic and endoscopic cooperative surgeries (LECS) may possibly change the treatment for the duodenal tumors to more safe and feasible one. LECS for GI tumors have recently been developed (8). Currently, the LECS concept has rapidly permeated for treatment of GI tumor due to its certainty and safety, although there is still room for improvement to lessen its technical difficulty.

Per-oral endoscopic myotomy (POEM) was introduced by Minami *et al.* as an endoscopic myotomy with no skin incision for achalasia that is a benign but long-lastingly symptomatic esophageal motility disorder resulting from an impaired relaxation of the lower esophageal sphincter, compromising the suffering patients' quality of life (9). The procedure has

been well accepted and widely applied owing to its minimal invasiveness and high cure rates. Clearly, POEM as well as ESD require extensive training and its reiteration for archiving proficiency, and idealistically, a trainee is to perform the procedure under close supervision and mentoring of experienced endoscopists who offers adequate advice on site whenever necessary. If this is not the case, maybe in most hospitals, the harvested porcine GI tract organs are inexpensive, and a ready-to-use means to become used to handling the devices. The live porcine model simulates a more realistic setting of ESD, allowing trainees to climb their learning curves in a shorter time (10). For its future success, a rigorous training system for currently state-of-art endoscopic techniques is warranted to be established and standardized. To address this issue, Sato *et al.* developed a novel *ex-vivo* POEM training model. The model was developed using polyvinyl alcohol hydrogel which can easily be modified to reproduce the stiffness of the different intestinal layers, namely the mucosa, submucosa and muscle layer (11). Thus, non-biomaterial model has the feasibility to provide an effective endoscopy education tool and a satisfactory training experience. We believe that the global dissemination can be a great boon for much more patients suffering from GI neoplasia or intractable benign disorders.

This special issue has also dealt with progresses in endoscopic treatment for distal malignant biliary obstruction and gastroduodenal outlet obstruction and a unique topic of new photodynamic therapy with next-generation photosensitizers. Please seize the near or foreseeable future that endoscopic therapies are ever-changing strategies and never-ending challenges for GI neoplasia and the refractory conditions.

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