ORIGINAL ARTICLE

Gut and Liver, Vol. 8, No. 6, November 2014, pp. 619-624

The Feasibility of Using Simulated Targets in the Stomachs of Live Pigs for Full Endoscopic Submucosal Dissection Training

Horng-Yuan Wang*[,†,‡,§], Shou-Chuan Shih*[,†,‡,§], Chien-Yuan Hung*[,†], Chia-Yuan Liu*[,†,‡,§], Tze-Yu Shieh*[,†], and Ming-Jen Chen*[,†,‡,§]

**Division of Gastroenterology, Department of Internal Medicine, Mackay Memorial Hospital, Taipei, †Department of Nursing, Mackay Junior College of Medicine, Nursing, and Management, Taipei, ‡Clinical Skills Training Center, Department of Medical Education, Mackay Memorial Hospital, Taipei, and §Department of Medicine, Mackay Medical College, New Taipei, Taiwan*

Background/Aims: In endoscopic submucosal dissection (ESD) training, only a flat target lesion can usually be simulated in the normal mucosa. This study aimed to evaluate the feasibility of simulated targets in the stomachs of live pigs for complete training. **Methods:** Six trained endoscopists with hands-on experience with *ex vivo*, isolated pig stomachs were enrolled in this pilot study. An endoscopic banding device was used to create a polyp that was snared, leaving an ulcerated lesion. This simulated target model was used to perform ESD in pigs. The *en bloc* resection rate, procedure time, complications, quality of resection, and participants' opinions on the simulated targets were compared with the conventional model. **Results:** *En bloc* resections were achieved in all six simulated targets and six conventional models. The mean size of the resected specimens was 32.2 mm (range, 20 to 39 mm) in the simulated target group and 23.5 mm (range, 11 to 40 mm) in the conventional group. The target model had a high quality of resection and had a high satisfaction rate for margin identification and correct peripheral marking. **Conclusions:** Good identification of the lesion and ease of periphery marking in the target model may improve resection quality. **(Gut Liver 2014;8:619-624)**

Key Words: Animals models; Gastroscopy; Gastric mucosa; Dissection; Swine; Competency-based education

INTRODUCTION

Endoscopic submucosal dissection (ESD) is a standard technique for performing *en bloc* resection of early digestive neoplasms and has been widely accepted.[1] However, ESD is a very operator-dependent technique involving several skills and different instrumentation. The learning curve from novice to learner to competent level should be systematic and supported by adequate training programs. A panel of experts from Europe reached a consensus that the minimum training requirement to achieve the competent level was hands-on experience and management of complications in live pigs.[2]

In the usual training protocol, only flat lesions can be simulated in the normal mucosa. The lesion is made by suction of the mucosa, or with a needle-type knife or argon plasma coagulation. This approach can cause some drawbacks for trainees. For example, trainees may lack the experience to make proper and safe margins from the flat lesion.[3] We previously developed a novel method with a simulated target in *ex vivo* systems using isolated pig stomach (modified compact the Erlangen Active Simulator for Interventional Endoscopy [EASIE] model) for variable subtype lesions in polypectomy or ESD training.[4,5] The *ex vivo* model, however, cannot simulate the opportunity to respond to potential complications of bleeding and perforation. The aim of this study was to evaluate an adaptation of this concept to simulate targets in the stomach of live pigs for full ESD training. The novel approach of this pilot study has not previously been described.

MATERIALS AND METHODS

1. Baseline participants' characteristics and training experience

Six endoscopists who were of comparable age, with a mean age of 34 years (range, 32 to 35 years), and academic background (second year fellow or first year attending) were enrolled in the study. They had previously undergone a systematic ESD training program in our clinical skills training center and animal laboratory. They received a didactic session about the indications, proper techniques, and equipment settings for ESD.

Correspondence to: Ming-Jen Chen
Division of Gastroenterology, Department of Internal Medicine, Mackay Memorial Hospital, No. 92, Sec. 2, Chungshan North Road, Taipei, Taiwan
Tel: +886-2-25433535 (ext. 2260), Fax: +886-2-25433642, E-mail: mingjen.ch@msa.hinet.net

Received on August 30, 2013. Revised on October 13, 2013. Accepted on October 14, 2013. Published online on April 23, 2014
pISSN 1976-2283 eISSN 2005-1212 http://dx.doi.org/10.5009/gnl13327

They then received hands-on experience, including the use of an artificial tissue model and at least four to six sessions of isolated pig stomach. None of them had ever practiced ESD in patients.

2. Preparation of pigs for ESD

Three pigs (male, Landrace, *Sus scrofus domesticus*; weight 28 to 30 kg) were provided from our animal center. The pigs were fasted for more than 12 hours before the ESD procedure. All the endoscopic procedures in pigs were performed under general anesthesia. An overtube (ST-C3; Olympus Optical Co., Ltd, Tokyo, Japan) was used to prevent trauma of the larynx during multiple sessions of endoscopic insertion.

3. Creating simulated target lesions in live pigs

Depressed target lesions in live pigs were simulated to enable validation of a target for performing ESD.[6] Briefly, a pseudopolyp was created in the upper corpus of the pig stomach by using a pneumatically activated esophageal variceal ligation device (MD-48709; Sumitoma Corp., Tokyo, Japan) by a supervisor who had clinical experience of ESD. The supervisor transected the pseudopolyp with snare cautery, using "cut 1" mode at a power level of 100 (ESG-100; Olympus Optical Co., Ltd.) and left a mucosal defect to simulate a depressed target (Fig. 1A and B).

4. The study design and ESD techniques

The training program was approved by the Animal Care and Use Committee and the Institutional Review Board of Mackay Memorial Hospital (MMH-A-S-100-34).

The 4-hour training course was divided into two parts. 1) For the conventional model, a 10-mm normal gastric area was identified as the presumed lesion by the trainee. A needle knife was used for marking the periphery, which was set to about 5 mm outside of the lesions. 2) In the target model, a simulated target was created by the instructors and the trainee was asked to mark the periphery with 5 mm safe margins outside the target lesion. All six trainees performing the ESD undertook one session with the conventional model and one session with the target model in a similar position in the pig stomach.

The maneuvers for ESD were similar to the standard protocol in humans (Fig. 1C-F). In the present study, a water-jet gastroscope (GIF-Q260; Olympus Optical Co., Ltd.) was used. An ESG-100 (Olympus Optical Co., Ltd.) electrosurgical generator

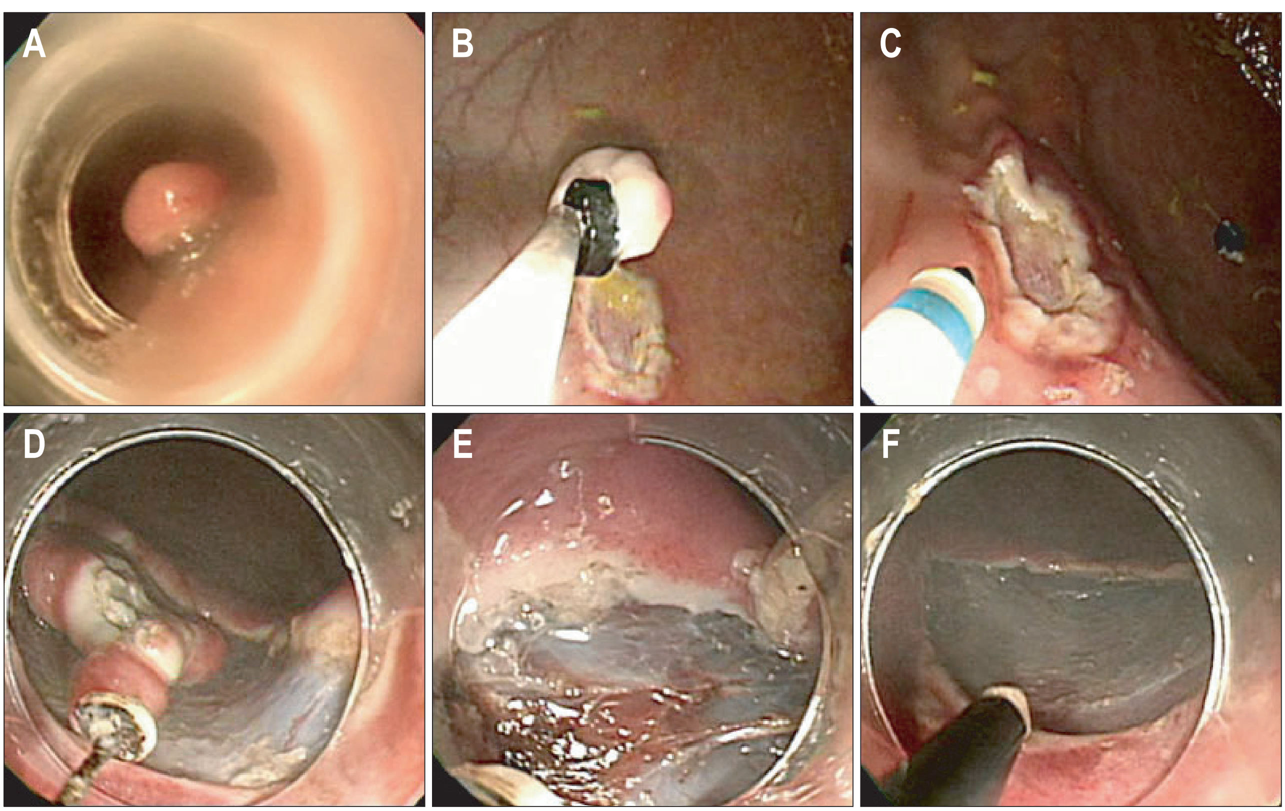

Fig. 1. A pseudopolyp was created in the upper corpus of a pig stomach using a pneumatically activated esophageal variceal ligation (A). The pseudopolyp was transected with snare cautery (B). A dual knife was used to mark the periphery, which was set to approximately 5 mm outside the target (C). A distal attachment cap was mounted on the tip of the gastroscope to enable a better endoscopic view and manipulation of the submucosal dissection. The mucosa outside the marking was initially precut and then circumferentially incised, and the submucosal layer under the lesion was dissected using an insulated-tip knife (D). A coagrasper was used when visible vessels or active bleeding were identified (E). The target lesion was completely resected, leaving an artificial ulcer (F).

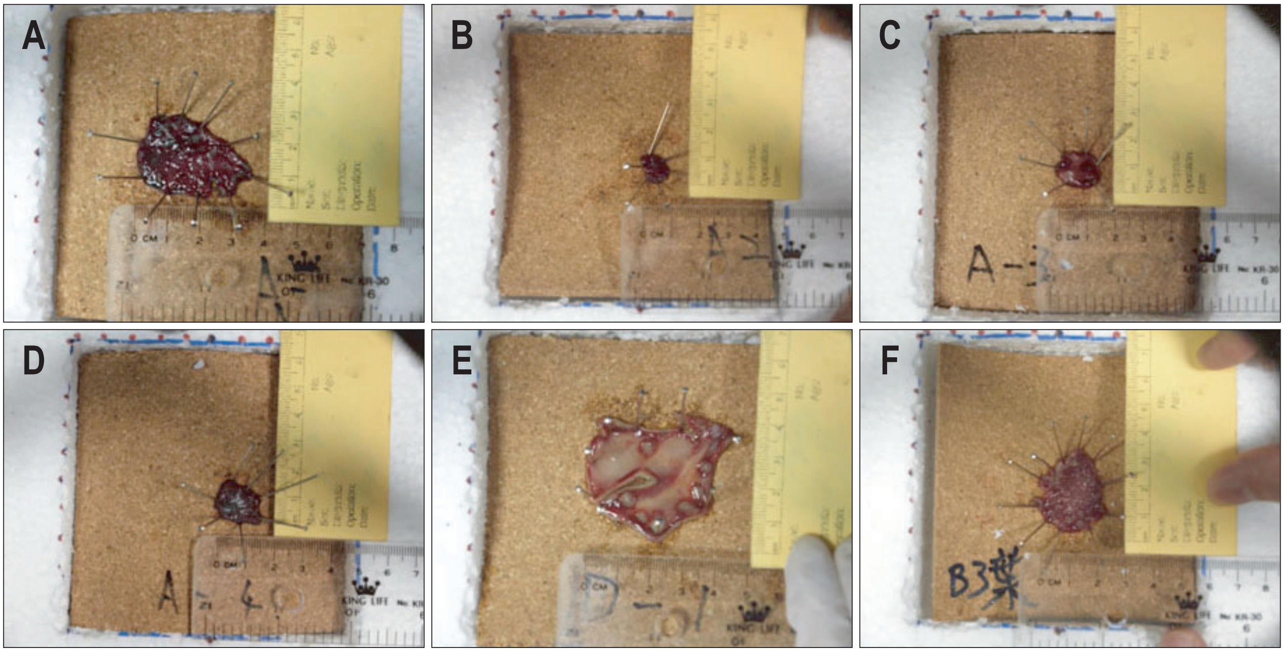

Fig. 2. Specimen samples using the conventional model. Poor quality resections have an irregular shape (E), an inadequate safety margin (B, C, D), or a cut in the lesion (E). (A) and (F) are considered as quality and complete resections.

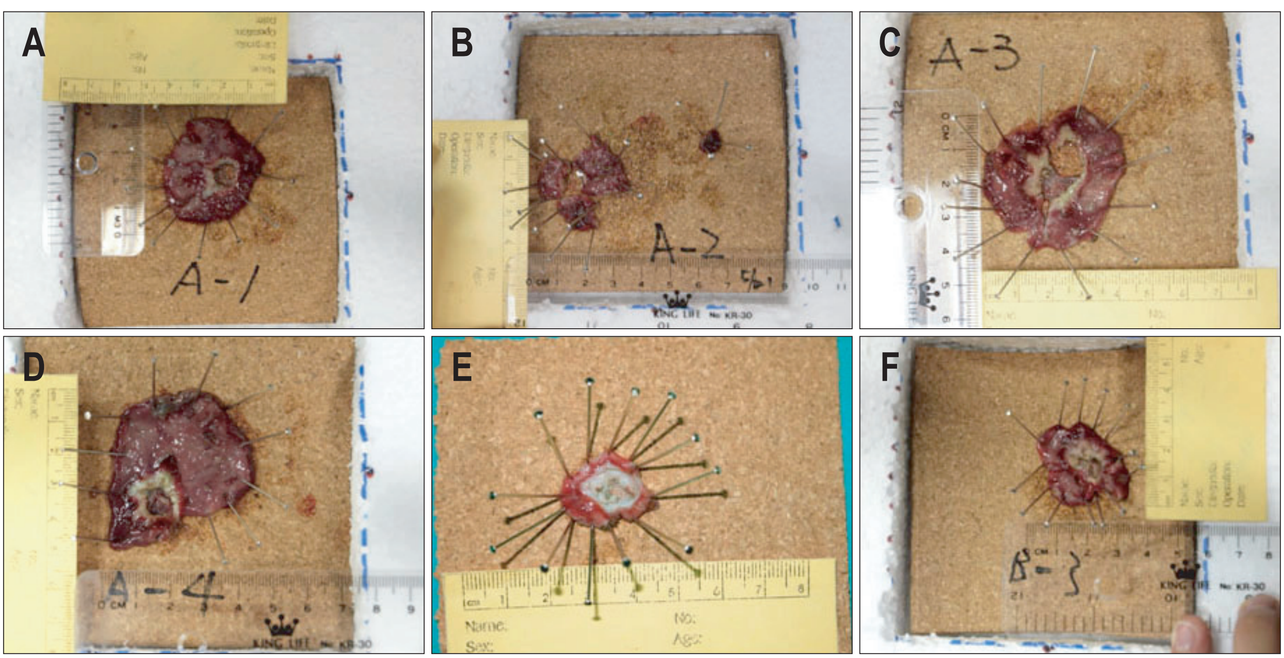

Fig. 3. Specimen samples using the target model. Poor quality resections have an irregular shape (B) or a cut in the lesion (B, D). (A), (C), (E), and (F) are considered as quality and complete resections.

was used in all the procedures, and the settings were changed according to the procedure being performed. For the initial marking, "force coagulation I" mode was used at power level of 50. During submucosal dissection, "pulse cut slow" mode was used at power level of 80. For coagulation with the coagulation grasper, "soft coagulation" mode was used at power level of 80. Normal saline mixed with epinephrine and indigo carmine was use for submucosal injection. To improve the endoscopic view and manipulation in submucosal dissection, a distal attachment cap (D-201-10704; Olympus Optical Co., Ltd.) was mounted on the tip of gastroscope. A coagrasper (FD-410LR; Olympus Optical Co., Ltd.) was used when visible vessels or active bleeding was identified. The specimen was then resected, pinned on a cork, and measured. Fig. 2 shows the specimens using the conventional model and Fig. 3 shows specimens using the target model.

5. Outcome measurements

The six trainees used both simulation models to achieve 12 resections on three pigs. The following variables were analyzed: size of specimens, *en bloc* resection rate, duration (time required from marking of the periphery until the specimen was resected), and the quality of the resection, including a regular shape, an adequate free margin of about 5 mm, and no cut in the lesion. The participants then completed a questionnaire regarding their opinions on the two models using a 5-point score from 1 (poor) to 5 (excellent) on each of the following aspects of both models: 1) identification of lesion; 2) marking of the periphery; 3) mucosal precutting; 4) submucosal injection; 5) submucosal dissection; and 6) management of complications. Given the small number of pigs in each group, statistical analysis of the data would be of questionable validity. For the purposes of this pilot study, however, we used descriptive statistics, reporting the means (±SDs) of the size of resected specimen, procedure time and participant's opinion score. These data were used for a rough comparison.

6. Statistical analysis

Given the small number of pigs in each group, statistical analysis of the data would be of questionable validity. For the purposes of this pilot study, however, we used descriptive statistics, reporting the means (±SDs) of the data. These data were used for a rough comparison of the size of resected specimen, procedure time and participant's opinion score.

RESULTS

1. Assessment of the procedure-related variables for conventional and target models

In total, 12 *en bloc* resections were achieved by six endoscopists. The mean size of the resected specimens was 32.5 mm (range, 28 to 38 mm) using the target model and 23.5 mm (range, 11 to 40 mm) using the conventional model. There were two major bleeding episodes (33%) in each group that needed to be coagulated with the Coagrasper during the ESD procedures. The mean time for the total procedure was 40.5 minutes (range, 28 to 52 minutes) using the target model and 38.2 minutes (range, 30 to 50 minutes) using the conventional model. There was no perforation or procedure-related mortality. A good quality of resection, including a regular shape, adequate margin, and no cut in the lesion, was achieved in 4/6 procedures using the target model and in 2/6 procedures using the conventional model (Figs 2 and 3). The target model had higher scores for identification of the margin (3.8±1.1 vs 2.7±0.8) and marking of the periphery (4.7±0.5 vs 3.7±1.4) compared to those for the conventional model from the participants' opinions. There were no differences in scores for mucosal precutting, submucosal injection, submucosal dissection, and management of complication.

DISCUSSION

The most important advantage of the new model is the ability to simulate targets in the stomach of live pigs for full ESD dissection training, including identification of the lesion, proper marking of a safety margin for the lesion, and managing complications, such as bleeding and perforation. The novel approach of this pilot study has not been described before.

The learning course from novice level to learner level to competence level is supported by adequate training programs in our institutional training protocol. We use artificial tissue for a novice level to provide ample opportunity for reuse.[7] Briefly, the artificial tissue is composed of a hook-and-loop fasteners. The upper layer consists of hairy loops and represents the submucosa, while the lower layer consists of hooks and represents muscle. When these layers are separated by pulling or peeling the two surfaces apart using a knife, it mimics the process of submucosal dissection. The isolated pig stomach is thought to be an excellent educational model for learner level for ESD training with a high degree of realism.[8-10] The isolated pig stomach has the advantage of the lack of ethics consideration of using live animals before achieving a competent level.

At present, training or developing new endoscopic techniques relies mainly on the live pig model, which has a stomach comparable in size and structure to the human stomach, to achieve a competent level.[11] Furthermore, the live pig model simulates a more realistic endoscopy setting and provides the opportunity to deal with bleeding and perforations. In previous training protocols, an imaginary lesion was first made to avoid losing track of the margins. However, only a flat target lesion was made in the normal mucosa by suctioning using the endoscope or by small cautery burns. This approach can cause some drawbacks for trainees. For example, the trainees may lack the ability to make proper and safe margins, which may bear the risk of inadequate treatment and incomplete resection.[12]

This has traditionally been accomplished by having trainees perform ESD in patients under close supervision by experts and timely hand-on practice. Of course, this is a good way and by no means will or can replace that. Despite the widespread use of ESD, apart from Japan and Korea, the clinical application of ESD remains low. This means that in the course of ESD training or clinical practice, the trainees apart from Japan and Korea is unlikely to have many opportunities to perform ESD. Therefore, another advantage of this animal training model is to provide repeated practice for trainees to overcome this steep learning curve.

In this study using the target model, the *en bloc* resections were achieved in all six simulated targets with two major bleeding episodes (33%) and no procedure-related mortality. The mean time for total procedure was 40.5 minutes (range, 28 to 52 minutes). ESD is being increasingly recognized worldwide as a definitive therapy. The goals of definitive therapy include the completed *en bloc* resection and the removal of eccentrically-shaped lesions with a safe margin. Though there were no difference of the *en bloc* resection and complication between the targets and conventional models. The target model had a high quality of resection and had high satisfaction rates for margin identification which are necessary for a definitive treatment. Our pilot study demonstrates the feasibility of using the live pigs for full ESD training, whether those results will translate into better clinical performance remains to be seen.

Teoh *et al.*[13] used the live porcine model without a target lesion in an ESD training workshop for 24 novice endoscopists in Hong Kong. They achieved similar results as in the present study. Their novice endoscopists, however, need a longer procedure time of 52 minutes and caused a higher rate of bleeding and perforation during 13 ESDs (56.5%). The better outcome from our pretrained endoscopists may be because they had already learned to perform ESD in our *ex vivo* model training.

The expense of conducting hands-on training on live animals may be a limiting factor for some training programs. Our 4-hour live animal training program costs about US $300 per trainee, including the instruments used to create the lesions and perform the ESD (US $100), and the animals and animal facility charges (US $200, two trainees share an animal). The endoscopes and accessories were instruments that had been retired from clinical practice and cost almost nothing to use. Therefore, we believe that this live porcine simulator should be used only for achieving the competent level to gain the experience of full clinical practice. This may raise the question of how many procedures should trainees do in *ex vivo* isolated stomachs before they transition to the live animal model? In our trainees, when they achieve success in four to six ESDs of *ex vivo* isolated stomachs, they reach the learner level to enable progression to performing the live animal procedure.

Finally, what should be the criteria for transition from animals to clinical patients? We have no clear answer yet. Some experts have stated that the minimum training requirement should be five ESDs in live pigs and the ability to manage complications.[2] It would be preferable to conduct a study on a larger scale with an appropriate sample of trainees and make recommendation.

This pilot study provided an almost complete opportunity for full ESD training, but there were some differences from the situation in clinical practice in the mucosal thickness, submucosal vascular suppleness, and electrocoagulation settings. The pig stomach appeared to be thicker and harder than a human stomach because the submucosal injection was frequently more difficult to accomplish. The blood supply in the submucosal layer was less prominent in the pig stomach than in the human stomach, and the possibility of bleeding during the ESD procedure was about 33%, which was less than expected. In addition, the electrocoagulation power settings need to be set differently for clinical practice in humans.

There are a number of limitations in this pilot study. The first, giving the small number of pigs in each group, statistical analysis of the data would be of questionable validity. For the purposes of this pilot study, we used descriptive statistics for a rough comparison. Second, we could not create a lesion larger than 10 mm using an esophageal variceal ligation device. It may be difficult to resect a lesion with a maximum diameter of 5 cm in 30 minutes, as suggested to be the training goal by some experts.[2] Third, the freshly created 0-IIc lesions do not behave in the same way as fibrosed, ulcerated gastric cancer, which are more technically difficult for the ESD procedure.

In conclusion, the evaluation of the method we devised showed the feasibility of simulated targets in the stomach of live pigs for full ESD training. Comparing the target model with the conventional model, the mean procedure time and complication rate were similar between the two groups. The target group had a higher rate of quality resection with a regular shape, adequate safe margin, and no cuts in the lesion, which means a complete resection. These findings may contribute to the better utilization of the target model especially with regard to identification of margin and proper marking of the periphery.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

ACKNOWLEDGEMENTS

The authors thank the colleagues in the Animal Center and Clinical Skills Training Center for preparing the live pig model and providing technical assistance.

REFERENCES

1. Gotoda T, Yamamoto H, Soetikno RM. Endoscopic submucosal dissection of early gastric cancer. J Gastroenterol 2006;41:929-942.
2. Deprez PH, Bergman JJ, Meisner S, et al. Current practice with endoscopic submucosal dissection in Europe: position statement from a panel of experts. Endoscopy 2010;42:853-858.
3. Kim EY, Jeon SW, Kim GH. Chicken soup for teaching and learning ESD. World J Gastroenterol 2011;17:2618-2622.
4. Chen MJ, Lin CC, Liu CY, et al. Training gastroenterology fellows to perform gastric polypectomy using a novel ex vivo model. World J Gastroenterol 2011;17:4619-4624.
5. Wang TE, Wang HY, Lin CC, et al. Simulating a target lesion for endoscopic submucosal dissection training in an ex vivo pig model. Gastrointest Endosc 2011;74:398-402.
6. Chen MJ, Liu CY, Chen CJ, Shih SC, Wang HY. Simulating target lesion for endoscopic submucosal dissection training in live pig model. Endoscopy 2012;44 Suppl 2 UCTN:E300-E301.

7. Wang HY, Shih SC, Hung CY, et al. Use of artificial tissue to practice endoscopic submucosal dissection. Endoscopy 2013;45 Suppl 2 UCTN:E175-E176.
8. Parra-Blanco A, Arnau MR, Nicolás-Pérez D, et al. Endoscopic submucosal dissection training with pig models in a Western country. World J Gastroenterol 2010;16:2895-2900.
9. Yamasaki M, Kume K, Yoshikawa I, Otsuki M. A novel method of endoscopic submucosal dissection with blunt abrasion by submucosal injection of sodium carboxymethylcellulose: an animal preliminary study. Gastrointest Endosc 2006;64:958-965.
10. Haycock AV, Youd P, Bassett P, Saunders BP, Tekkis P, Thomas-Gibson S. Simulator training improves practical skills in therapeutic GI endoscopy: results from a randomized, blinded, controlled study. Gastrointest Endosc 2009;70:835-845.
11. Parra-Blanco A, Nicolas D, Arnau MR, Gimeno-Garcia AZ, Rodrigo L, Quintero E. Gastric endoscopic submucosal dissection assisted by a new traction method: the clip-band technique. A feasibility study in a porcine model (with video). Gastrointest Endosc 2011;74:1137-1141.
12. Gotoda T, Friedland S, Hamanaka H, Soetikno R. A learning curve for advanced endoscopic resection. Gastrointest Endosc 2005;62:866-867.
13. Teoh AY, Chiu PW, Wong SK, Sung JJ, Lau JY, Ng EK. Difficulties and outcomes in starting endoscopic submucosal dissection. Surg Endosc 2010;24:1049-1054.