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A local structured training program with live pigs allows performing ESD along the gastrointestinal tract with results close to those of Japanese experts

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ABSTRACT

Background and aims: The high specific skill needed by ESD limit its widespread use in Europe and animal training is recommended in Europe to improve the results of ESD that are far from Japanese at present. We create a local training program using live pigs as models, along with our human cases, to provide continuous exposure to the technique.
Methods: Between February 2013 and December 2015, two young operators performed 55 pig gastric ESDs in parallel with 62 human cases for large superficial cancerous lesions. The number and training dates of pig cases were adapted to those of the human cases to achieve continuous exposure to ESD cases.
Results: The en bloc, R0, and curative resection rates were 100%, 85.5% (53/62), and 77.5% (48/62), respectively with no recurrence observed during the one year follow up. There was no statistically significant difference in terms of the R0 or curative resection rates among ESDs performed during 2013–2015 (R0: 80% vs. 86.6% vs. 86.4%; Curative: 80% vs. 86.6% vs. 73%).
Conclusion: A local structured training program using live pig models was used to train endoscopists for ESD in humans with high safety and efficiency, similar to results published by Japanese experts.

1. Introduction

Endoscopic submucosal dissection (ESD) has become the standard of care for large superficial gastrointestinal neoplasms [1]. However, the technique involves new and unusual endoscopic skills. This explains the long and flat learning curve, reflecting poor results of physicians inexperienced in ESD, with reports of higher complication rates and lower R0 resection rates.

ESD originated in Japan, where superficial cancerous gastric lesions are endemic; however the classic mentor-apprentice teaching model could not be applied in Western countries [2] because of well-known epidemiological differences and because of a lack of experts [3]. Consequently, in 2010, the European Society of Gastrointestinal Endoscopy (ESGE) published minimal training requirements [4] prior to initiating ESD in Europe: at least five gastric ESD procedures had to be performed on animal models (ex vivo or in vivo) and at least 15 live procedures had to be observed in expert centers. No clear recommendations yet exist but the benefit of training models [5–12] (in vivo and ex-vivo) has been reported in a lot of papers.

Moreover, according to the ESGE [4], ESD should initially be performed at the rectal site, because of the higher number of cases involving this site in Western countries, the relative safety of the

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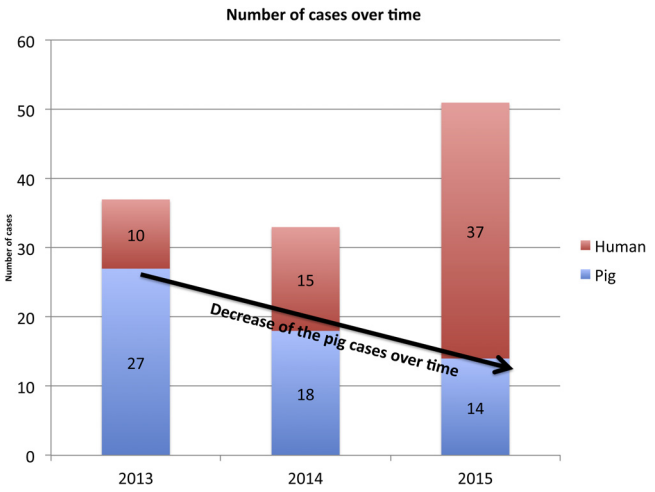

Fig. 1. Number of cases over time.

procedure due to its location under the peritoneal reflection, and the difficulty and morbidity of the surgical alternative. Regular subsequent practice of the ESD procedure is required to increase success and decrease the procedure time and complications.

Despite these recommendations, the first results published by Western teams fell short of those obtained by Japanese experts, with an R0 resection rate between 50 and 80% in European studies, far below the 90% reported by Japanese experts [3].

After a negative experience with our first rectal ESD involving a case of a lateral spreading tumour of the middle rectum (7-h procedure time, piecemeal resection at the end of the procedure), which occurred despite following the European recommendations [4], we decided to initiate a structured local training program with continuous and regular exposure to gastric ESD in in vivo pigs, performed in parallel to our human cases.

2. Materials and methods

2.1. Operator experience

Between February 2013 and December 2015, 55 pig gastric ESDs were performed by two young operators (30 and 32 years old at the beginning of the study) in a total of 16 anaesthetised pigs. The more experienced operator was able to autonomously perform interventional endoscopy (ERCP, diagnostic and therapeutic EUS, more than 100 EMR along the gastrointestinal tract) whereas the younger operator was still in training. The operators had each performed five animals ESDs before the beginning of the study.

2.2. Design of the study

After seven pig gastric ESDs, the older operator felt confident to begin human rectal ESDs, whereas the younger operator felt confident after 11 pig gastric ESDs. This "confidence" level was subjectively evaluated by the feeling of being able to perform ESD with good efficacy (en boc resection >80%, R0 resection >70% and perforation rate <10%). In total, 62 human ESDs for large precancerous and superficial cancerous lesions were performed during the study period. In addition, 44 animal ESDs were performed in parallel to maintain continuous exposure to ESD cases (Fig. 1).

2.3. Organization of the training program

In total, 27 pig ESDs were performed during the first year (2013), 18 during the second year (2014), and 10 during the last year (2015) (Fig. 1). The number of pig cases and the training dates were adapted to those of the human recruitment to achieve continuous exposure to ESD cases.

Taking the pig and human cases together, 34 ESDs were performed in 2013, 33 in 2014, and 47 in 2015. The mean number of ESDs per month was 2.8 in 2013, 2.75 in 2014, and 3.9 in 2015 (Fig. 1). The proportion of pig ESD cases decreased with an increase in recruitment: 79.4% during the first year (2013), 54.5% during the second year (2014), and 21.2% during the last year (2015).

2.4. Animal portion of the study

Domestic Landrace mini-pigs (20–25 kg) that fasted 48 h before the procedure were used for the study. Premedication was performed with intramuscular ketamine (11 mg/kg). Gastric ESDs were performed under general anaesthesia, induced and maintained with intravenous propofol with oro-tracheal intubation. This study was approved by the Institutional Animal Care and Use Committee.

All gastric ESDs were performed using a Hybridknife type T (Erbe medical, Tübingen, Germany), injecting either a glycerol mixture (glycerol 10%, fructose 5%, NaCl 0.9–85%) or normal saline solution, dyed with indigo carmine. A virtual standardised gastric lesion in the corpus or the antrum of the stomach was created using a polypectomy snare using a soft coagulation current (effect 5, 80 W).

The two operators performed all ESDs using an upper gastrointestinal endoscope (Karl Storz 13821PKS; Karl Storz Endoscopy, Tuttlingen, Germany) with a distal cap attached (4-mm length and 3-mm diameter side hole; D201-11304; Olympus, Tokyo, Japan). An endocut Q current (effect 2) was used for the circumferential incision whereas swift coagulation current (effect 4, power 50 W) was used for submucosal dissection. A VIO 200D (Erbe medical, Tübingen, Germany) was used as an electro-surgical unit. One anaesthetised mini-pig allowed between two and five gastric ESDs during a day or half-day of procedures.

The specimen size was measured at the end of the procedure and was defined by the two diameters using the ellipse formula [13]: area (mm^2) = (small diameter (mm)/2) × (large diameter (mm)/2) × π. Duration was defined as the time between the first marking around the virtual lesion to the end of the dissection and allowed calculating the dissection speed (mm^2/min). The perforation and bleeding rates were also recorded. Bleeding was considered a complication when haemostatic forceps (Coagrasper FD-411 UR; Olympus America Inc., Miami, FL, USA) were needed to achieve haemostasis.

2.5. Human portion of the study

During the same period, 62 large precancerous and superficial cancerous lesions were treated by ESD in the university hospital of Limoges, France (43 rectal lesions, 12 oesophageal lesions, and 7 gastric lesions). A pretherapeutic EUS was performed systematically to eliminate any invasion of the submucosal or the muscular layer and to confirm the absence of regional lymph node metastasis even if no adenocarcinoma was determined by pretherapeutic biopsies. A high-definition video-endoscopy was also performed systematically, with an analysis of the lesion using white-light endoscopy and narrow-band imaging to search for macroscopic signs of submucosal invasion that could contraindicate the ESD.

All except the first five were performed by the two operators, who took turns every hour to expedite the procedures. All procedures were performed using a Hybridknife type T, injecting normal saline solution during the first five procedures and glycerol mixture for the next 57 procedures. All steps involved in the ESD (marking, injection, circumferential incision, submucosal dissection) were performed with the Hybridknife type T using a high-definition video-gastroscope (GIF 190, Olympus) with an accessory channel

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