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Review Article

Establishing a submucosal endoscopy program in a gastrointestinal unit

Poornima Varma¹ and Payal Saxena^{2,*}

A B S T R A C T

Establishing a submucosal endoscopy program in a new unit is a difficult but exciting task. There are several key steps and teams involved in the success and failure of this endeavour. Careful thought, planning and implementation at the start will allow an easier transition to the development and progression of this program. An interested gastrointestinal unit with skilled proceduralists holds the key to the commencement of a submucosal program. The opportunity for ongoing learning and training through animal models and simulations, are important for proceduralists to continue to enhance their skills and train other staff. A collaborative team with surgical, nursing and technical support, hospital board approval, and credentialing, as well as the acquisition of appropriate equipment are essential components.

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Keywords: Gastrointestinal unit; Per-oral endoscopic myotomy; Submucosal endoscopy; Training

Introduction

Therapeutic endoscopy is a fast-growing field with technical advances in diagnostic and therapeutic endoscopy in luminal disease. One of the key advances in the last 10 years has been the birth of third space endoscopy.^{1,2} Third space endoscopy evolved from the concept of natural orifice transluminal endoscopic surgery (NOTES) which was described in 2004 on porcine models³ and then in humans when Rao and Reddy⁴ performed the first human NOTES appendicectomy. After a hiatus through technical limitations in its application, the access to previously feared spaces and planes morphed into an expansive field of therapeutic potential.

The knowledge of this third space gave way to the description of submucosal endoscopy with mucosal flap safety valve technique and its application in animals in 2007 by Sumiyana et al and Pasricha et al.^{5–7} This technique was a way to access this submucosal plane and peritoneal cavity and safely close the defect using a mucosal flap. The following year, Inoue et al⁸ performed the first human per-oral endoscopic myotomy (POEM) using the same method. The ensuing evolution gave way to a vast range of applications (Table 1), including gastric POEM (G-POEM),⁹ Ze-

nker's diverticulum POEM (Z-POEM),¹⁰ oesophageal diverticular POEM (D-POEM),¹¹ POEM with fundoplication (POEM-F),¹² and further broadened applications to endoscopic submucosal dissection (ESD), submucosal tunneling endoscopic resection (STER) or per-oral endoscopic tunneling resection (POET),^{13,14} per-oral endoscopic tunneling restoration of oesophagus (POETRE),¹⁵ per-rectal endoscopic myotomy (PREM),¹⁶ and peritoneoscopy.⁷

Performing these procedures with high levels of technical and clinical success requires a skilled operator. In addition to operator proficiency, the program setup consists of several steps (Table 2) including acquisition of appropriate equipment, nursing training, and education, multidisciplinary team involvement, surgical support, institutional, and credentialing board approval.^{17,18} The endoscopist should also continue development of their skills through attendance at endoscopy courses and academic meetings.

Unit Based Requirements

Proceduralist training

The first step in developing any submucosal program is for the proceduralist(s) to acquire skills in performing submucosal

¹Department of Gastroenterology, Austin Hospital, Heidelberg, Australia²AW Morrow Gastroenterology and Liver Centre, Royal Prince Alfred Hospital, Camperdown, Australia

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* Corresponding author. AW Morrow Gastroenterology and Liver Centre, Royal Prince Alfred Hospital, Missenden Rd., Camperdown, NSW 2050, Australia.
E-mail address: psaxena1@jhm.edu (P. Saxena).

Table 1 Techniques in Submucosal Endoscopy

Technique	Indication
ESD	Resection of gastric, oesophageal or rectal lesions
POEM	Treatment of achalasia
Z-POEM	Treatment of Zenker's diverticulum
D-POEM	Treatment of oesophageal diverticulae
POEM-F	Treatment of achalasia plus fundoplication
STER/POET	Treatment of gastrointestinal subepithelial tumours
POETRE	Management of oesophageal strictures
PREM	Treatment of Hirschsprung's disease

ESD, endoscopic submucosal dissection; POEM, per-oral endoscopic myotomy; Z-POEM, Zenker's diverticulum POEM; D-POEM, oesophageal diverticular POEM; POEM-F, POEM with fundoplication; STER, submucosal tunneling endoscopic resection; POET, per-oral endoscopic tunneling resection; POETRE, per-oral endoscopic tunneling restoration of oesophagus; PREM, per-rectal endoscopic myotomy.

endoscopy. Through available training pathways and programs, local proceduralists have the opportunity to upskill. The availability of an animal laboratory for training with pig models not only allows the proceduralist to continue and enhance their skills, but also gives opportunity for other medical and nursing staff to gain familiarity in the newer techniques.

The basic operator requirements to be able to perform these procedures includes expertise in upper gastrointestinal (GI) endoscopy, colonoscopy, endoscopic mucosal resection (EMR), and ESD.¹⁹ It may be desirable to have experience in endoscopic ultrasound as well. In addition to endoscopic dexterity, an understanding of the tissue planes is vital for performing dissection of the submucosa and muscular layers.¹⁹ Furthermore, the proceduralist must be proficient in managing any adverse events which may arise while performing submucosal endoscopy, primarily bleeding and perforation. The proceduralist should be familiar with various homeostatic techniques, placement of through the scope and over-the-scope clips, and placement of enteral of stents which may be required when performing third space procedures.

Training methods

Eastern model

Historically, the Japanese model of training in ESD is a Master-Apprentice model which takes years to perfect.^{20,21} This model involves self-initiated learning through conference and workshop attendance, case conferences, and didactic teaching.^{21,22} This generally occurs alongside case-based learning through observation of ESD procedures by mentors and procedural assisting. Subsequently, the trainee begins to perform parts of the ESD procedure, progressing onto smaller lesions in the upper GI tract. Once competency in gastric and oesophageal ESD is accomplished, the trainee will progress to colorectal ESD.^{21,22}

This model is highly effective; however, not easily applicable to Western countries^{20,21} due to lower incidence of early upper GI lesions thereby providing Asian trainees with far greater volume of experience compared to their Western counterparts. There are also limitations in training itself where the Japanese institutions have the opportunity to train full-time fellows as compared to Western countries where advanced endoscopists self-initiate their training, and often have less time to devote to this extensive training program.

Table 2 Basic Requirements in Establishing a Submucosal Program

Skilled endoscopists
Training models and workshops to train staff
Specific and appropriate equipment <ul style="list-style-type: none"> • ESD knives • Coagulation forceps • Haemostatic devices • TTS clips • OTSC • Enteral stents • Electrosurgical units
Multidisciplinary team involvement
Surgical support
Institutional and credentialing board approval
Nursing support
Tertiary referral network

ESD, endoscopic submucosal dissection; TTS, through-the-scope; OTSC, over-the-scope clips.

Western model

Due to the limitations mentioned above, the Western training model has adapted the training requirements of the Eastern model and have recommended an alternate comprehensive and complementary approach to training. The model includes multiple steps in the learning pathway.^{20,21} The most crucial step is self-study through literature, books, and online videos to gain basic understanding of submucosal techniques, their efficacies, as well as safety and risk profiles. The use of endoscopy simulators including *ex vivo* and animal models, artificial tissue and virtual reality simulators provides a deeper understanding of tissue planes, albeit do not allow a true appreciation of the interaction with live tissue. The observation of live cases, nationally and internationally, enhances that understanding by observing the variability between patients and their anatomy, the interactive nature of the GI tract with diaphragmatic movement, vascular networks and bleeding, and management of unforeseen adverse events. Where physical observation is not possible, long distance learning through tele-mentoring, video coaching and training apps can assist with the live case learning and troubleshooting. Finally, hands-on training courses through conferences, ESD workshops and ESD training programs encompasses the last of the recommended training model employed by Western countries. This model is a more theory-based approach to training prior to establishing practice as compared to the highly clinical and technical hands-on Eastern model.

Pig model

There are several similarities between pig and human stomach which provides a good platform for learning on tissue itself,²¹ but there are also key differences such as thinner oesophageal layers, different anatomy, and decreased vascularity which creates an 'easier' submucosal plane for dissection.^{17,23,24} Many training centres have set up animal training models and workshops as a starting point for proceduralists who may not have had much experience in submucosal endoscopy. As mentioned, however, there are limitations to pig model training which do not allow appreciation of the variable nature of the live patient, and therefore does not solely prepare the proceduralist for the management of unexpected differences and adverse events in live human cases which require prompt action. Two published series have reported outcomes of experienced endoscopists attending ESD courses with practical

pig model stations with perforation rates of 22%–65%.^{20,25,26} This highlights the importance of live hands-on experience to appreciate complexity and deal with the narrow spaces, vasculature, and thin layers in living, breathing, and bleeding patients.

Observing an expert

Observation of an expert performing live ESD cases is important and quite valuable in the training of any proceduralist. Trainees are often encouraged to approach local and national experts to observe their practice and familiarise themselves with the technique. However, given the limitations in Western countries as discussed, the number of cases performed at Asian high-volume centres provides remarkable exposure and understanding of these in a shorter time span.²¹ Therefore, short-term observational fellowships, even as short as a 1–2 weeks²¹ to centres such as in Japan add value and would almost be essential in submucosal endoscopy training.

Proctored procedures

A useful step prior to commencing independent submucosal procedures is inviting an expert proctor to supervise the initial human case(s). In an international survey on POEM experience by Stavropoulos et al,²⁷ it was shown that only 9 out of 16 centres reported having an expert proctor present for initial cases; however, where present, the median number of cases proctored were two prior to commencing procedures independently. The added guidance and support provide the proceduralist with necessary confidence and validation of the newly acquired cognitive and technical skillset. Mastery of POEM technique in particular, is evidenced by a decrease in the length of the procedure, variability in the minutes per centimeter of myotomy and in the incidence of inadvertent mucosotomies.²⁸ The learning curve is reported as low as 20–40 cases; however, recent US data suggests approximately 250 cases per proceduralist is required with continued improvement in resection rates seen beyond 300 cases.^{27–31} The survey opinion suggested introducing proctoring for first live human cases as a mandatory requirement for new proceduralists as part of their accreditation.²⁷

There is considerable variability in the training models used by international centres that have established their POEM programs and also the extent of pre-clinical training undertaken by their proceduralists on *ex vivo* models, live animals and cadavers.²⁷ The total hours of pre-clinical training is reported to range from 12 to 154 hours;²⁷ however, given the complexity of these techniques, the greater the pre-clinical cognitive training, the greater the confidence to deal with anatomical and procedural variability, patient factors and complications. These models, therefore, either in part or in ideally in combination, form the foundation for the required training and experience for proceduralists wishing to gain expertise in submucosal endoscopy and establish a program in their unit.

Staff training

Upon completion of training, it is the responsibility of the proceduralist to set the foundation for training within the institution. This usually involves the development of animal models, live-training workshops, and teaching endoscopy sessions. Establishing these training opportunities within the unit also gives opportunity the primary proceduralist(s) to continue their own training on-site and improve their practice.

One of the key staff in these procedures are the endoscopy nursing staff, as the technical success of the procedure in part re-

lies on their understanding and application of the equipment and accessories. It is therefore important to ensure that there is opportunity for them to familiarise themselves with the accessories used in each procedure. Most of the submucosal techniques utilize different equipment settings or unfamiliar products, such as knives, coagulation forceps, haemostatic products, and electrosurgical generators (Table 3).^{2,18} Education sessions outside of a patient-setting will allow procedure and equipment training in a stress-free environment.

Once the necessary education sessions are completed, staff can gain further confidence and understanding of these procedures and the equipment through learning cases. These are selected low complexity live cases, where adequate procedural time is allocated for teaching during the case, allowing opportunity for discussion and clarification.

Location is also vital as these should be conducted where the proceduralist and team are most comfortable. Most centres would perform these procedures in the endoscopy unit where there is access to accessory equipment, trained nursing staff and potentially other endoscopists. However, initial human cases may be performed in the operating theatre given the potential for surgical support.

Multidisciplinary teams

The third key requirement is multidisciplinary team involvement with surgeons, gastroenterologists and in some cases, oncologists and pathologists. Cohesion between teams allows valuable discussion on the roles and timing of each team's involvement along the patient's journey, with often a fine line between endoscopic or surgical intervention. Collaboration with surgical teams, particularly upper GI surgeons will be valuable in determining the best treatment plan for the patient as well as support for the management of any adverse events.

Institutional approval

Once the framework for training is established and key medical teams are in support, the program relies on institutional and credentialing board approval.^{17,18} This involves a stakeholder meeting on the aims of a submucosal endoscopy program and benefits to the patient population and to the hospital.¹⁸ The presence of endoscopic, gastroenterological, and surgical heads of

Table 3 Examples of Equipment and Accessories Required in Submucosal Endoscopy

Equipment	Model and manufacturer
Endoscope	GIF-HQ190; Olympus (outer diameter of 9.2 mm, integrated water channel)
Electrosurgical generators	VIO 300 D; ERBE ESG-300; Olympus
Electrosurgical knives	Triangle Tip Knife (KD-640L; Olympus) HybridKnife (20150-060; ERBE) Triangle Tip Knife J (KD-645L; Olympus) HookKnife (KD-620LR; Olympus) ITknife2 (KD-611L; Olympus)
Coagulation forceps	Coagrasper (FD-410/411UR/412LR; Olympus)
Haemostatic products	SURGICEL Absorbable Hemostat Product (Ethicon) Resolution clip (Boston Scientific)

Data from the article of Nabi et al (*Gastroenterol Hepatol (N Y)*. 2018;14:224–32).²

department and program directors is required. Accreditation and credentialing of the procedures can be difficult as there are no set guidelines or requirements for proceduralists prior to performing these procedures.¹⁸ Education of the administrative team with evidence and references to international training models, learning curves and reputable institutional practices can assist with credentialing.

Submucosal Procedures

ESD

Understanding the anatomy of GI wall layers and working with mucosal planes is best understood through ESD. This is a well-established technique for curative resection of early or pre-cancerous lesions within the upper and lower GI tract.^{20,21} It involves a) mucosal marking around the lesion, b) submucosal injection to lift the lesion, c) circumferential incision, d) submucosal dissection, and e) *en bloc* retrieval of the resected lesion.²¹ A meta-analysis of 15 studies demonstrated ESD was associated with higher *en bloc* and curative rates (odds ratio [OR], 13.9 and 3.5, respectively) compared to EMR^{20,32} for oesophageal, gastric, and colorectal neoplasms. There were also lower recurrence rates after ESD of both malignant and pre-malignant lesions across all study groups (OR, 0.09).^{20,32} However, ESD procedure durations were longer with higher risk of bleeding and perforation (OR, 2.20; OR, 4.09, respectively) compared with EMR. With superior outcomes coupled with higher adverse events, it makes it imperative that proceduralists performing these have access and opportunity to necessary training in the field.

POEM

POEM has become an established therapeutic option for patients with oesophageal motility disorders. Achalasia is a primary oesophageal motility disorder characterized by absent peristalsis of the oesophageal body and failure of relaxation of the lower oesophageal sphincter.³³ There are 3 types of achalasia; type 1 where there is no significant pressurisation in the distal oesophagus, type 2 with pan-oesophageal pressurisations, and type 3 with at least 20% of swallows showing rapidly propagated pressurisation or spastic simultaneous contractions.^{34,35} Since its development in 2007, POEM has revolutionized the treatment of achalasia, which until now was limited to Botulinum toxin injection, pneumatic dilatation, and/or surgery. There is now over 8 years of published evidence on the safety and efficacy of POEM in the management in achalasia^{36,37} with high clinical success rates. A recent systematic review on POEM reported high clinical efficacy (> 90%), an improvement in quality of life, a reduction in lower oesophageal sphincter pressures and reductions in Eckardt scores.³⁴ There was a reportable reduction on hospital length of stay with POEM procedures in general as compared to Heller's myotomy, with a cost analysis favouring POEM.³⁴ There is also evidence in spastic oesophageal disorders with clinical success found to be 92% in type 3 achalasia, 88% in diffuse oesophageal spasm and 72% in Jackhammer oesophagus.³⁸ The growth in the evidence of POEM has resulted in a shift in the treatment algorithm of oesophageal motility disorders, with more proceduralists and institutions accepting its utility in practice and therefore, expanding their endoscopic skills.

POEM subtypes

Given its value and clinical success, variations of POEM are emerging and have shown promise in endoscopic management of similar difficult conditions including refractory gastroparesis, oesophageal and Zenker's diverticulum, and reflux post-POEM. In a review of seven studies on G-POEM, Khoury et al³⁹ have reported technical success in 100% of cases, clinical efficacy in 81.5% and normalisation of measures in gastric emptying studies in 55.5% of cases, with complications between 6.6% and 7.6%. The findings support its efficacy and use in the treatment of gastroparesis after failure of conventional therapy. Similarly, in early studies on D-POEM and Z-POEM^{7,40,41} have shown comparable results. An early US and Chinese collaborative study of 11 patients with oesophageal diverticulae undergoing D-POEM found technical success rates of 90.9%, clinical success rates of 100% with a decrease in mean dysphagia score from 2.7 to 0.1 ($P < 0.001$) during a median follow-up of 145 days.⁴⁰ In the management of Zenker's diverticulae with Z-POEM, an international study of 75 patients conducted by Yang et al⁴¹ showed overall technical success rates of 97.3%, clinical success in 92% and a decrease in mean dysphagia score from 1.96 to 0.25 ($P < 0.001$). There were 4 perforations in this cohort, and at 12-month follow-up, only one patient reported symptom recurrence. Prospective long-term data of these techniques are awaited.

STER/POET

Endoscopic resection of subepithelial tumours in the GI tract can be performed by the STER or POET procedure via submucosal tunneling techniques. The technique was first described by Xu et al⁴² in 2012. The lesion can be dissected and removed by the use of alternative electrocautery knives to dissect and detach the lesion and then remove it via polypectomy snares, prior to closure the mucosal defect.^{7,43,44} Subsequently, several cohort studies have evaluated the role of STER/POET.^{7,13,14,45-51} The largest reported by Chen et al¹⁴ of 180 patients with upper GI submucosal tumours with *en bloc* resection rate of 90.6% and complication rate of 8.3%. All patients remained free from local recurrence and distant metastasis at median follow-up of 36 months. In comparison to thoracoscopic enucleation, STER/POET have shown equal efficacy, shorter procedure times, favourable post-operative, and long-term outcomes.^{7,14,45}

Other submucosal procedures

Two other novel techniques include POETRE and PREM. POETRE is aimed at restoring luminal patency in patients with post-radiation and post-surgical stenoses.^{7,15,52} It involves two endoscopes entering the submucosal plane antegrade through the mouth and retrograde through a gastrostomy port to tunnel through the fibrosis and meet the opposing endoscope. Where the two endoscopes meet, the tunnel wall is incised so that an exit to the lumen distal to the stenosis is opened. The luminal continuity is secured with temporary metal stent. In early study of 4 patients who underwent POETRE, there was reported improvement in dysphagia with a mean dysphagia score of 4 before the procedure to 2.5 afterwards (mean follow-up, 27.8 weeks).^{7,15,52} All patients, however, required serial dilatations as a consequence of metal stenting. Further studies are warranted as to its efficacy and associated morbidity in the medium to long-term.

PREM is a newer technique developed for the management of Hirschsprung's disease. The initial feasibility procedure was

termed per-anal endoscopic myotomy for the treatment of internal anal sphincter achalasia.⁵³ After the initial success, Bapaye et al¹⁶ performed a PREM for short-segment Hirschsprung's disease in a 24-year-old male over a total colonic length of 20 cm. At 24-week follow-up, the patient reported improvement in symptoms.

Conclusion

Developing a submucosal program is a challenging and exciting task starting at the level of endoscopist training and proficiency. This requires an intensive training program with varying Eastern and Western models to learn from. Once skilled in ESD and POEM, proceduralists are capable of developing their skills further in other submucosal techniques as described. There is then opportunity for roles to be reversed allowing the proceduralist or the 'Apprentice' to become the 'Master' and teach colleagues, junior medical and nursing staff at their own institutions to start forming the foundation for their own submucosal unit, alongside the necessary surgical and administrative support.

Conflicts of Interest

Poornima Varma has no disclosure. Payal Saxena is a consultant for Boston Scientific and ERBE.

ORCID

Poornima Varma, <https://orcid.org/0000-0002-5204-9338>

Payal Saxena, <https://orcid.org/0000-0003-3097-6314>

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