

Untutored learning curve for endoscopic submucosal dissection in New Zealand

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ABSTRACT

INTRODUCTION: Endoscopic submucosal dissection (ESD) is a specialised endoscopic technique in the treatment of large pre-cancerous and early cancerous gastrointestinal lesions that avoids the need for surgical resections. The objective of this study was to assess the feasibility, efficacy and safety of learning ESD in an untutored approach in a prevalence-based setting within New Zealand.

METHODS: Over a 4-year period, 80 ESD procedures were performed at a single tertiary centre within New Zealand. We retrospectively reviewed basic demographics of the patients, along with successful *en bloc* resection rates, dissection speeds, histological diagnoses (including margin assessments) and complications.

RESULTS: We captured 80 procedures. Within this database we achieved an *en bloc* resection of 88.7% (71 out of 80 cases) and an R0 resection of 72.5% (58 out of 80 cases). The international benchmark for dissection speed of 9cm²/h was achieved within the first block of 20 cases and was maintained throughout. There was a perforation rate of 6.25% (five patients), with one patient (1.25%) requiring emergency surgery for a rectal perforation.

CONCLUSIONS: Our study shows it is feasible and safe to learn ESD within a low-volume tertiary centre within New Zealand via a prevalence-based approach. The majority of patients were able to have *en bloc* resection and a R0 resection. Our intent is that this data be used to help design a more formalised training process for learning ESD within a New Zealand setting.

Endoscopic submucosal dissection (ESD) is an organ-preserving surgery performed for *en bloc* resection of pre-cancerous and early cancerous gastrointestinal (GI) lesions with a curative intent.¹ It has been performed in Japan since the 1990s and is now increasingly acquired by Western countries for management of early GI cancers.² It allows *en bloc* resection of the lesions and higher rates of R0 resection (clear vertical and radial margins histopathologically), which may result in curative resection of these cancers and preclude need for radical surgery or any other additional treatment.³

There is no structured programme for training in ESD in New Zealand. There is no screening programme for detection of early gastric cancer in New Zealand, which is considered an ideal target for commencement of ESD training. There is also a higher risk of complications with ESD in comparison to endoscopic mucosal resection (EMR). These factors have contributed to poor uptake of ESD in New Zealand and in Western countries in general.⁴

Studies from high-volume Japanese centres with a structured training programme with availability of gastric lesions suggest early ESD

proficiency is acquired after 30–40 procedures; however, in a Western setting with much lower volumes, achieving the same number of procedures in the setting of unstructured training is usually not possible.^{5,6} Data from Western countries show that dissection speed and *en bloc* resection rates continuously improve during the course of 40 to more than 100 procedures.^{4,7–9}

The aim of this study is to assess the learning curve of ESD applicable to the New Zealand setting where ESD is currently performed untutored. This study can serve as a useful guide to devise a training programme for ESD in New Zealand.

Methods

A prospective database of all ESD procedures is maintained at Middlemore Hospital, a tertiary referral centre in Auckland, New Zealand. We retrospectively analysed the outcomes for all consecutive ESD procedures performed by a single endoscopist (AS) over a 4-year period from February 2019 to January 2023. We captured patient demographics, location of the ESD, specimen size, *en bloc* resection rates, R0 resection rates, dissection speed and complications. We

analysed the learning curve using the accepted international benchmarks.

Patient selection

All cases put forward to undergo ESD were discussed at a multidisciplinary meeting (MDM). The majority of cases were referred with intent of curative resection; however, some cases were referred for staging, rather than for curative intent. These were cases with unclear level of invasion on imaging but suspected, based on endoscopic appearances, to be beyond cure with ESD.

Operator experience and training

The operator had 7 years' experience of performing extensive endoscopic mucosal resection throughout the GI tract. Preclinical training for ESD included the operator observing approximately 10 live cases of ESD being performed by Japanese and European experts. Following this, ESD was practised in *ex vivo* models (approximately 8 hours) and live porcine models (approximately 20 hours). The operator also watched more than 100 hours of ESD case videos in entirety performed by Japanese experts.

The first ESD procedure was carried out in February 2019. Each ESD procedure was videoed in its entirety. The first 15 cases were sent to local expert in ESD (CS), who reviewed each case and provided feedback directly to the operator after each ESD.

ESD procedure

Procedures were undertaken using either conscious sedation with fentanyl and midazolam or under general anaesthesia. Oesophageal and gastric lesions were marked prior to ESD and lifted with standard lifting solutions. Colorectal lesions were not marked and were lifted with standard lifting solution. ESD was performed using DualKnife J (Olympus America). The ESD bed was examined carefully post-procedure and haemostasis was achieved with thermal coagulation using the knife or coagulation graspers. Intraoperative perforation was closed using either standard clips or over-the-scope clip (Ovesco OTSC®).

Endoscopic outcomes and definitions

En bloc resection was defined as removal of the lesion in a single piece. For carcinomas, R0 resection was defined as a resection specimen with radial and deep margins clear of dysplasia or cancer, while R1 was defined as a specimen with

presence of dysplasia or cancer at the margin. A curative resection was defined as per European Society of Gastrointestinal Endoscopy guidelines.¹⁰ For non-cancerous lesions R0 resection was considered curative. For cancerous lesions the definition of a curative resection was more complex, defined as R0 with absence of vascular and lymphatic involvement, low tumour budding and a varying limit of depth of invasion according to the location and histology of the lesion. For oesophageal squamous cell carcinoma (SCC) the depth of invasion deemed to be curative was <200 µm from muscularis mucosa, for oesophageal or gastric adenocarcinoma the depth of invasion deemed to be curative was <500 µm from muscularis mucosa and for colorectal adenocarcinoma the depth of invasion deemed to be curative was <1000 µm from muscularis mucosa.¹⁰

Pathological specimen review

Each ESD specimen was pinned to a corkboard, placed in formalin, processed and then reviewed by a specialised GI pathologist (MY). Histology was reported with assessment of radial and deep margins for all lesions to determine whether the resection met R0 criteria. In the case of a cancer, depth of invasion of cancer was reported from muscularis mucosae along with tumour budding, cancer grade based on differentiation and presence or absence of lymphovascular invasion. Lesions were considered curative as per the definitions used for curative resection as above. All histology results were reviewed in an MDM.

Statistical analysis methods

Categorical data were presented as counts and proportions while continuous data were presented as means and standard deviations. We chose the internationally accepted benchmarks of dissection speed $\geq 9\text{cm}^2/\text{h}$, $\geq 90\%$ *en bloc* resection rate and $\geq 80\%$ R0 resection rate as markers to assess the proficiency of the ESD operator.¹¹

ESD duration (in hours) was estimated as the time between submucosal injection and specimen retrieval, and dissection speed was estimated as dissection lesion size (in cm^2) divided by ESD duration. The average dissection speed for sequential 20-case blocks was calculated, and the trend was shown by using a 20-case moving average graph. In addition, the rates of *en bloc* resection and R0 resection were further calculated for sequential 20-case blocks. A cohort bar plot was used to visualise average speed per case block and rates of *en bloc* and R0 resections in

comparison with the internationally accepted benchmark speed in different organs and case blocks. Furthermore, the Mann–Kendall test was implemented using *trend* R package in order to determine whether or not, overall, there was a monotonic trend in the dissection speed of the single operator.¹² R programming language version 4.3.1 was used to carry out these analyses.¹³

Results

We retrospectively analysed the outcomes for 80 ESD procedures performed by a single endoscopist over a 4-year period. The average age

of patients undergoing ESD was 68 years and 67.5% of our patients were male. The majority of patients were NZ European (57.5%), 15% were Asian, 16.25% were Pacific peoples and 5% were Māori (Table 1).

The 80 cases comprised 6 oesophageal, 20 gastric, 18 colonic and 36 rectal lesions (Figure 1).

Pathology

Adenocarcinoma comprised 25% of the cases (20 patients), with most of the remaining cases being made up of tubulovillous adenomas with low-grade dysplasia (18.8%, 15 cases) and tubular adenomas with low-grade dysplasia (18.8%,

Table 1: Demographics including age, gender and ethnicity of all patients undergoing ESD in our case series, as well as location.

	N (%)
Age	
<60	14 (17.5)
60–69	30 (37.5)
70–79	27 (33.75)
≥80	9 (11.25)
Gender	
Female	26 (32.5)
Male	54 (67.5)
Ethnicity	
European	46 (57.5)
Māori	4 (5)
Pacific peoples	13 (16.25)
Asian	12 (15)
MELAA	1 (1.25)
Other	4 (5)
Location	
Rectum	36 (45)
Stomach	20 (25)
Colon	18 (22.5)
Oesophagus	6 (7.5)

Figure 1: ESD cases by location—showing the majority of cases were undertaken in the rectum, with stomach being the next most common location, closely followed by colon, while oesophagus made up the fewest number of our ESD cases.

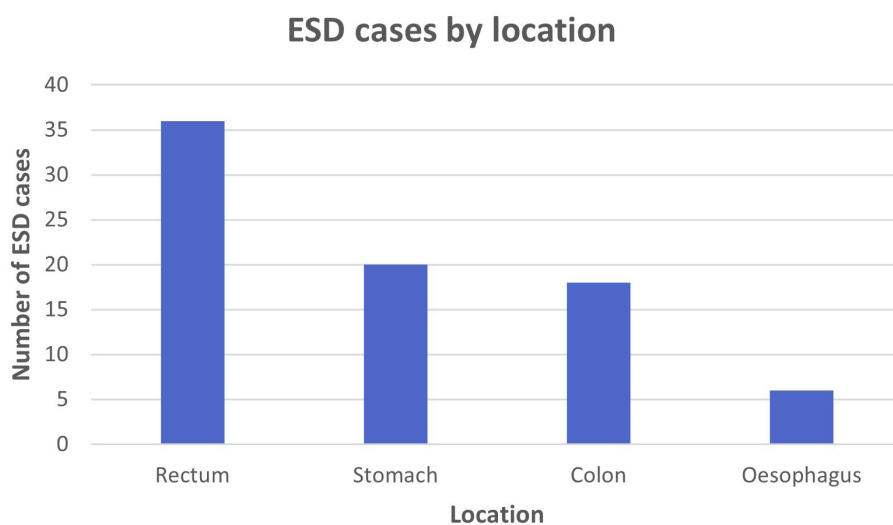
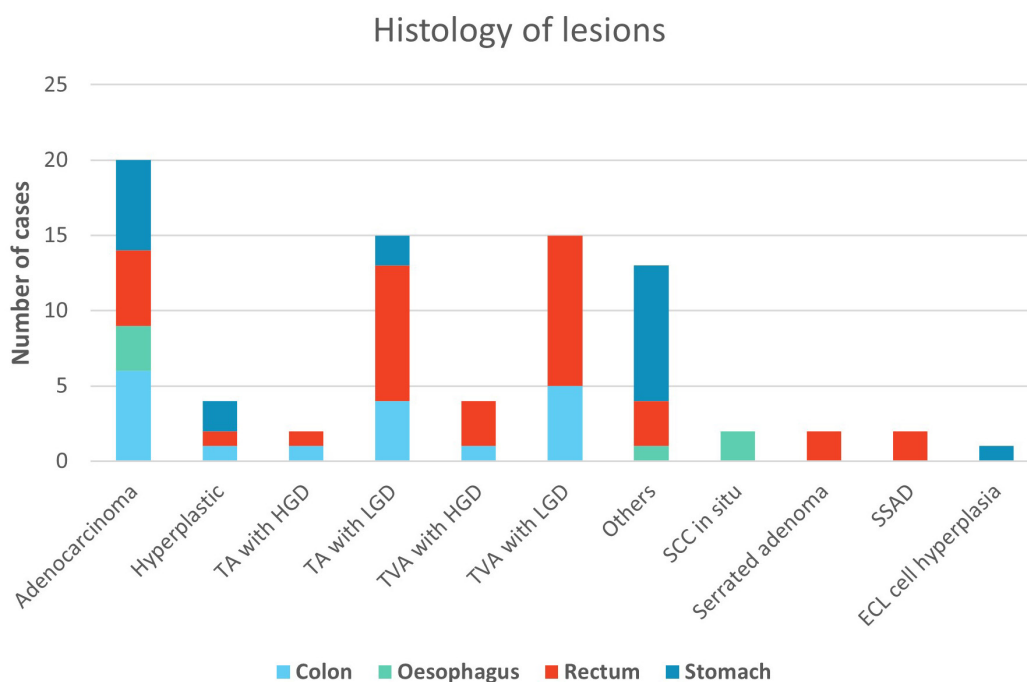


Figure 2: Histology of ESD-treated lesions by organ.



TA = tubular adenoma; HGD = high-grade dysplasia; LGD = low-grade dysplasia; TVA = tubulovillous adenoma; SCC = squamous cell carcinoma; SSAD = sessile serrated adenoma with dysplasia; ECL = enterochromaffin-like.

Figure 3: Average dissection speed calculated in 20-case sequential blocks, showing a statistically significant increase in the average dissection speed between the first and the last blocks.

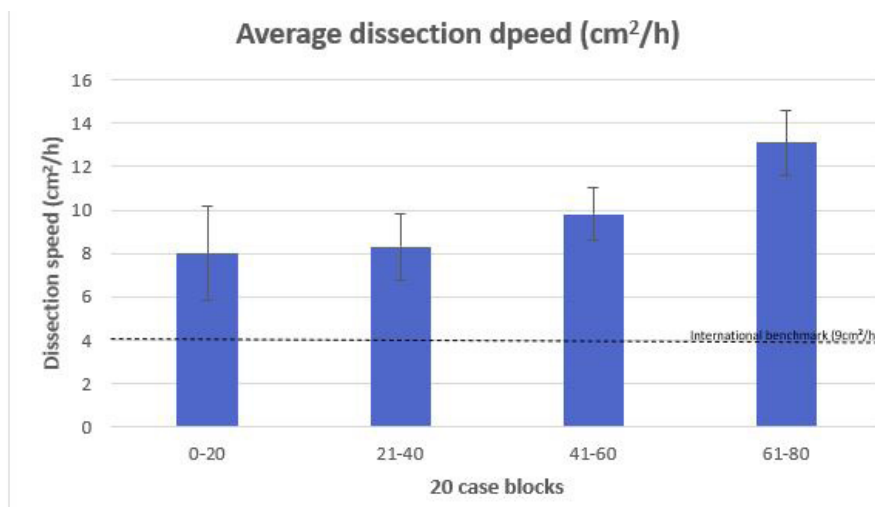
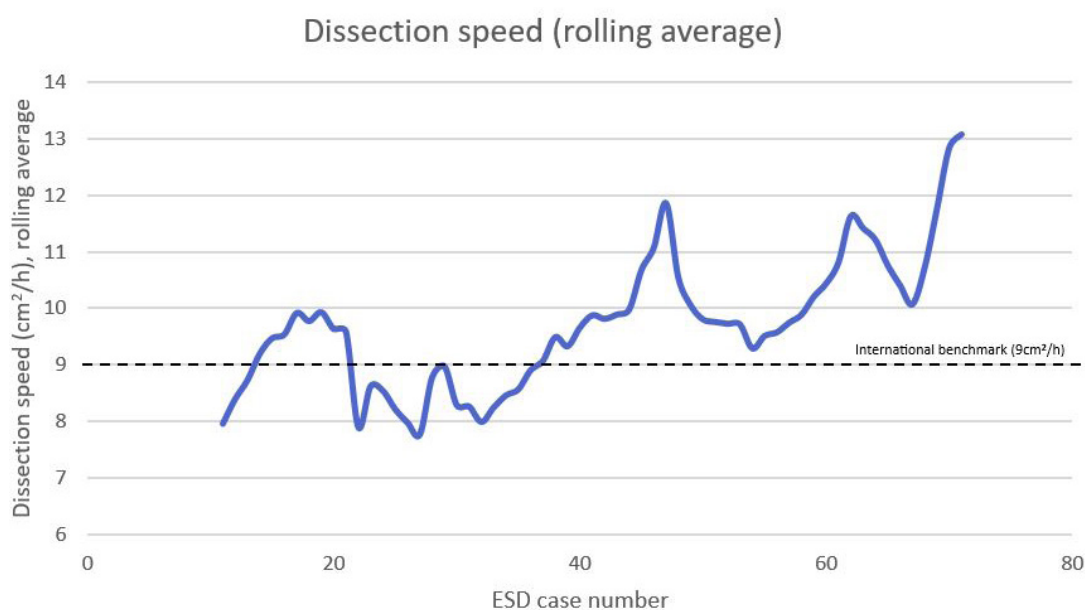


Figure 4: Dissection speed calculated as a rolling average, showing an increase in dissection speed as more ESD cases were completed.



15 cases). There were two cases (2.5%) of tubular adenomas with high-grade dysplasia and four (5%) cases of tubulovillous adenoma with high-grade dysplasia. There were small numbers of oesophageal SCC *in situ*, enterochromaffin-like (ECL) cell hyperplasia, serrated adenomas, hyperplastic polyps and sessile serrated adenoma with dysplasia (SSAD) (Figure 2).

Dissection speed

Our results have shown that average dissec-

tion speed increased sequentially as experience improved. This became statistically significant ($p=0.00002$) after 60 procedures and extended beyond the international benchmark in the 61–80 case sequential block (Figure 3). The moving average of dissection speed improved over time as the operator gained more experience (Figure 4).

The speed of dissection greatly varied between organs, with the fastest dissection speed being in colorectal lesions (Figure 5). This may be attributed to the fact that two thirds of the lesions

Figure 5: Dissection speed by organ, showing faster average dissection speed in colonic lesions compared to oesophageal ESD, as well as a trend towards significance for dissection speed in rectum and stomach lesions compared to colonic lesions.

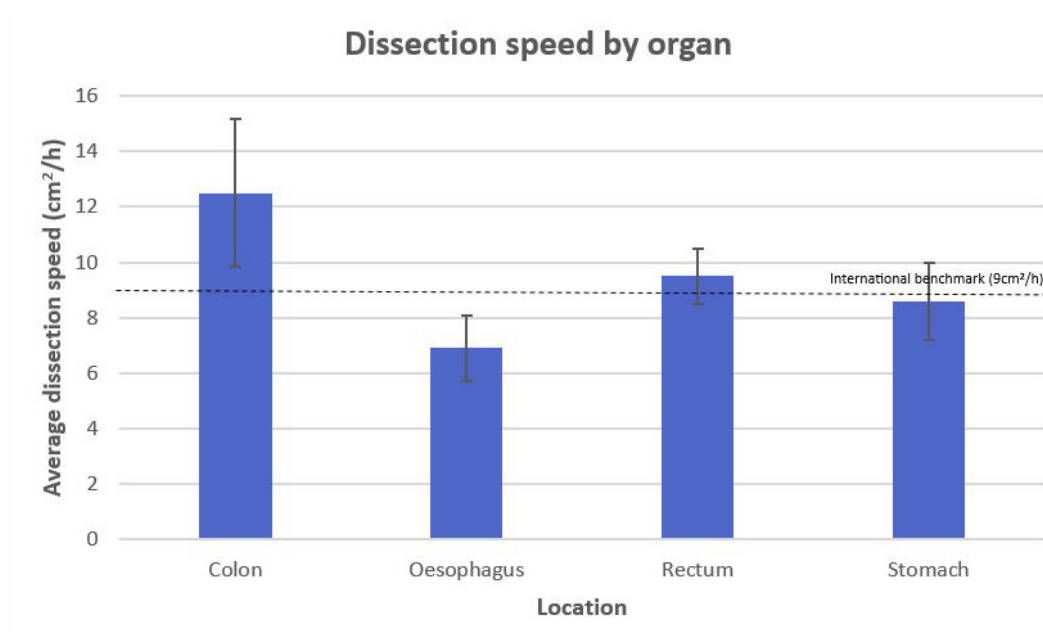
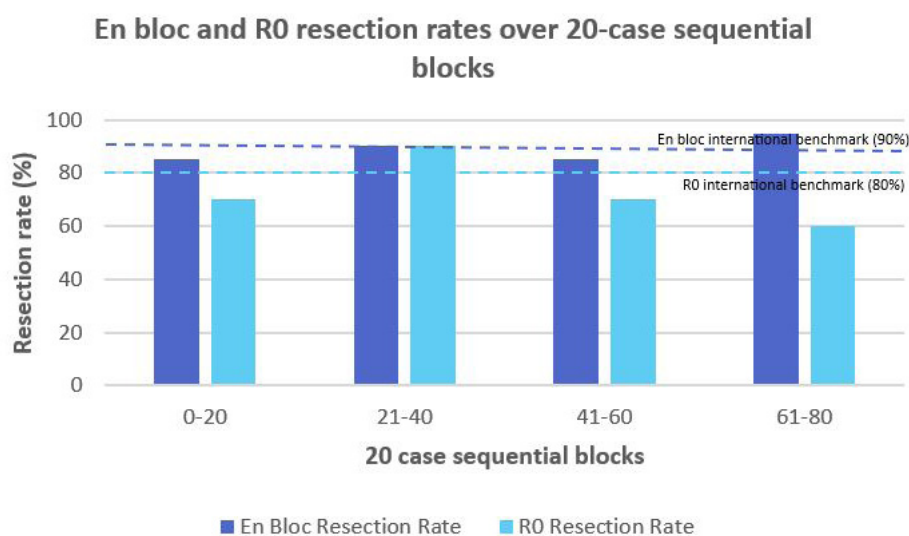


Figure 6: *En bloc* and R0 resection rates shown in 20-case sequential blocks with international benchmarks of 90% for *en bloc* resection rates and 80% for R0 resection rates included.¹¹



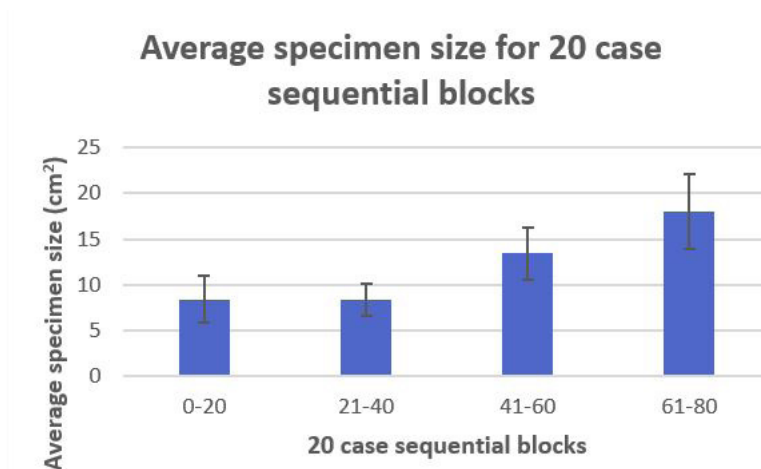
were colorectal, with more experience in treating these lesions potentially resulting in faster dissection speed.

En bloc and R0 rates

En bloc resection was possible in 88.7% of cases (71 out of 80 cases). In the remainder of cases, ESD

was converted to EMR to achieve full resection of the lesion. R0 resection was achieved in 72.5% of cases (58 out of 80 cases). A curative rate of 67.5% was achieved (54 out of 80 cases). There were several cases that were undertaken for staging purposes rather than curative intent, but these data were not captured prospectively.

Figure 7: Average specimen size, calculated in 20-case blocks, showing a continuous increase in size of specimens being resected. This could be due to larger lesions being accepted for ESD as operator experience and skill increased over time.



The *en bloc* resection rates achieved proficient level by the end of our series to above 90%. R0 resection rates met the international benchmark of 80% by the second block of 20 but dropped below this in the last two sequential blocks (Figure 6). This could be due to the fact the lesion size steadily increased ($p=0.002$) over 80 cases (Figure 7), more challenging cases were accepted for ESD, an increasing number of cases were accepted for staging purposes, or a combination of the aforementioned.

Complications

There was a perforation rate of 6.25% (five patients). Four of the perforations were recognised intraoperatively and closed with standard clips, received intravenous antibiotics and required no further intervention. One patient (1.25%) required emergency surgery for an unrecognised rectal perforation, undergoing a low anterior resection with a length of stay of 9 days. One patient (1.25%) had delayed bleeding requiring three units of blood but no endoscopic or surgical intervention. One patient (1.25%) had oesophageal stricturing after a circumferential oesophageal ESD, managed with serial dilations. Two patients had post-ESD inflammatory syndrome and were managed with antibiotics.

Eighteen patients (22.5%) were admitted to the hospital for observation after ESD for a mean of 2.3 days (range 1–9 days). There were no deaths in our cohort.

Discussion

This study demonstrates feasibility, efficacy and safety of an untutored, prevalence-based approach of a single operator. The slow uptake of ESD in the West, despite the advantages it offers over EMR, has been attributed to a lack of structured training programmes, a lack of suitable target lesions and a higher risk of complications with ESD.⁴ Many Asian countries such as Japan, on the other hand, have structured training programmes where trainees perform ESD under expert supervision, as well as an abundance of gastric lesions that are recognised as more suitable lesions for the initial learning curve of ESD due to the improved accessibility and thickness of the stomach layer.¹⁴ Consequently, proficiency in ESD in Western countries must be attained in an alternative fashion, as these settings are unable to provide the same environs available in countries such as Japan. A recent meta-analysis showed that *en bloc* and R0 resection rates in the Eastern studies were significantly higher at 95% and 89% respectively compared to Western studies where it dropped to 85% and 74% respectively. The percentage of perforations requiring surgery was significantly greater in Western countries (0.53%) compared to Eastern countries (0.01%). ESD procedure times were longer in Western countries (110 min vs 77 min).¹⁵

In most Japanese centres, trainees begin ESD on

gastric lesions. Oda et al. showed that 30 cases in the stomach were sufficient to gain competence in a supervised, tutored setting.⁵ The learning curve to achieve proficiency in colorectal ESD has been demonstrated. However, most operators in these studies had a prior experience of gastric ESD.⁹ Forty colorectal ESDs were required to gain competence with prior experience of gastric ESD. A study from Korea evaluated colorectal ESD training without prior experience in gastric ESD in a supervised setting. This study suggests that more than 100 cases are required to gain competence.¹⁶

These data, however, cannot be as readily applied to New Zealand, as there is no supervised training and the cases referred are a mix of oesophageal, gastric and colorectal lesions. Thus, an untutored prevalence-based approach is more realistic and pragmatic. Similar issues have been encountered in Europe and America. Untutored learning of ESD in Europe was first reported by Berr et al. performing ESD with a prevalence-based approach.¹⁷ The *en bloc* resection in the 50 cases evaluated in this study was 76%. Recent data from the US have shown that approximately 250 procedures are required to attain all parameters for ESD proficiency in all organs in an untutored, prevalence-based approach.⁴

We achieved the international benchmark of proficiency of *en bloc* resection rates and dissection speed with our ESD cohort. R0 resection rates are still below proficiency level; however, they are consistent with reported R0 resection rates at this level of ESD experience in Western studies.¹⁸ Our R0 resection rates may have been lower due to acceptance of more complex cases, larger size of the lesions in the latter part of the study and, in particular, cases accepted for staging where R0 resection is not an expectation.

Our complication rates were similar to those

reported Western studies but higher than studies from Japan.¹⁹ This may be attributable to our prevalence-based approach rather than gradual progression of easier gastric antrum lesions to more difficult lesions.

The strength of this study is that it demonstrates a real-world picture of the ESD learning curve in New Zealand. The prevalence-based approach is employed due to the case mix with variable lesion location and pathology, previously manipulated lesions and lack of supervision. Despite this, proficiency can be achieved safely with acceptable complication rates.

One of the limitations of our study is that it highlights the experience of a single endoscopist and may not translate to other endoscopists due to variability of technical skills and previous experience in advanced endoscopy. Nevertheless, similar models in Western studies have reported similar results.^{4,19} Regardless, it is likely that most larger centres in New Zealand will have only a few endoscopists who will take up ESD due to limited cases and this study will be generalisable to these centres.

Conclusion

Our study shows that there is a learning curve in ESD, with consistent improvement in dissection speed and *en bloc* resection rates in an untutored prevalence-based setting. Proficiency in ESD in most aspects can be achieved after 80 cases and is not site-specific. Higher numbers of ESD and careful lesion selection are required to reach the international benchmark for proficiency in R0 resection.

Finally, these data can help design the training programmes for ESD in centres where a prevalence-based approach is necessary.

COMPETING INTERESTS

Nil.

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